Genitourinary Masterclass

Best practice sharing: Practical approaches to patient care – Part 1

Prof. Jungmin Jo

South Korea

EV as first-line therapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer. Combination therapy with pembrolizumab.

EV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 or programmed death-ligand 1 inhibitor, and have received a platinum-containing chemotherapy

EV, enfortumab vedotin.
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July 2025 | Job code:MAT-KR-PAD-2025-00072

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Speaker disclosures

- Advisor for Janssen, MSD, Merck, BMS, and Astellas

BMS, Bristol Myers Squibb; MSD, Merck Sharp & Dohme

Introducing KJS

KJS

- Asian, male
- **Age: 77** years
- **ECOG PS: 1**
- **GFR: 43** mL/min
- **BMI: 20.57** kg/m^2
- **HbA1c: 6.7** mmol/mol (%)

Lifestyle:
Limited mobility due to pelvic pain

Employment status/job: Retired
Family history of cancer: None

Comorbidities: HTN, DM, Afib

Concomitant medications:
Amlodipine, carvedilol, sitagliptin, edoxaban

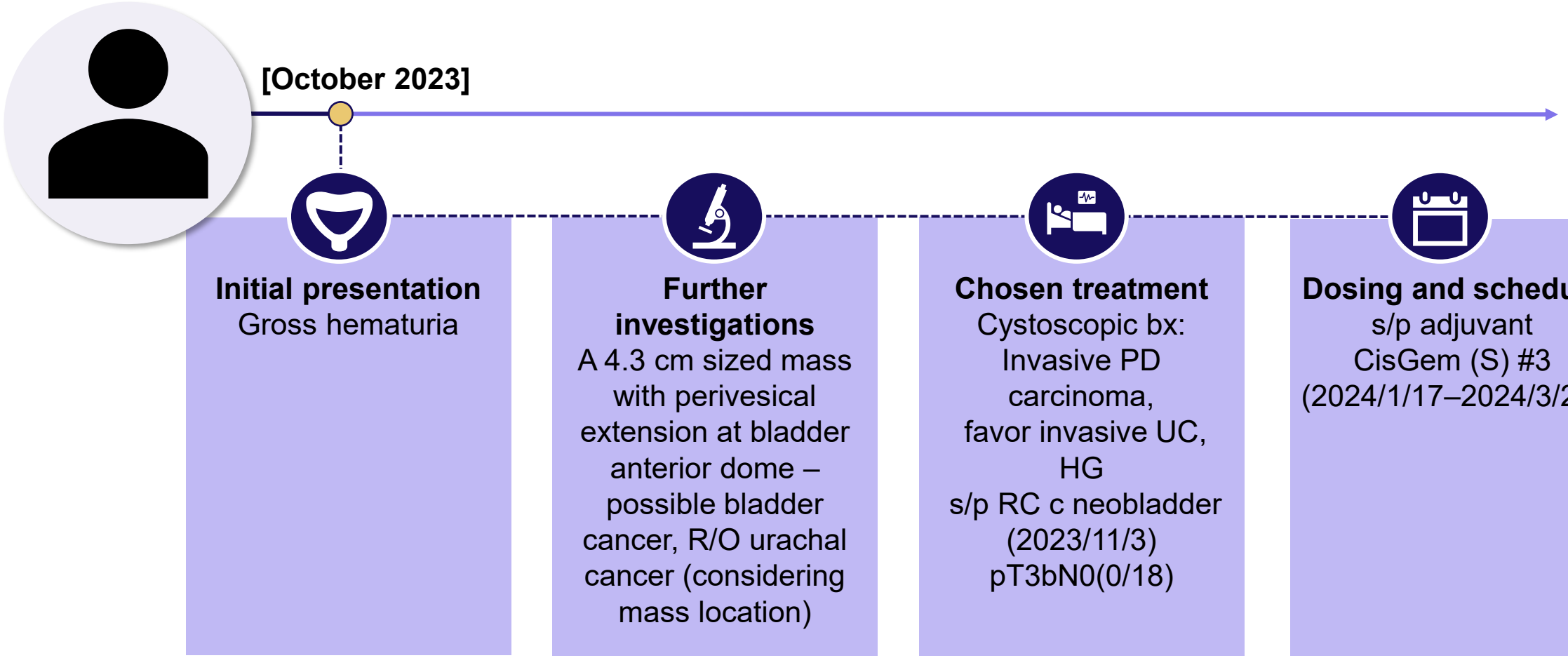
Any other relevant medical history:
Oral sodium bicarbonate for metabolic acidosis control

Habits:
Low physical activity due to cancer-related pelvic pain

Priorities:
Keen to receive life-extending treatment

Afib, atrial fibrillation; BMI, body mass index; DM, diabetes mellitus; ECOG, Eastern Cooperative Oncology Group; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; HTN, hypertension; PS, performance status.

Treatment initiation, dosage, and schedule



bx, biopsy; Cis, cisplatin; Gem, gemcitabine; HG, histological grade; PD, programmed death; RC, radical cystectomy; R/O, rule out; s/p, status post; UC, urothelial carcinoma.

Treatment initiation, dosage, and schedule

[April 2025]

Initial presentation
Right hip pain (3MA)

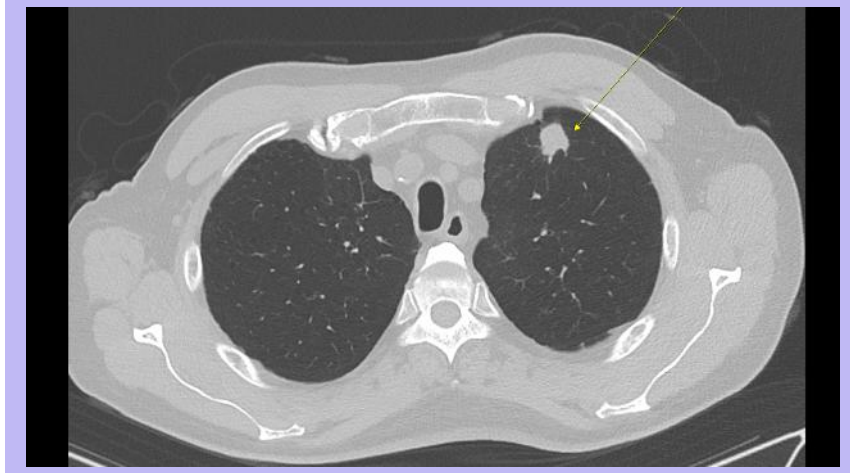
Further investigations
CT: Metastatic LNs in aortocaval area
Bone metastasis in left 8th rib, right 4th rib, L1, and right proximal femur
Lung metastasis in LUL

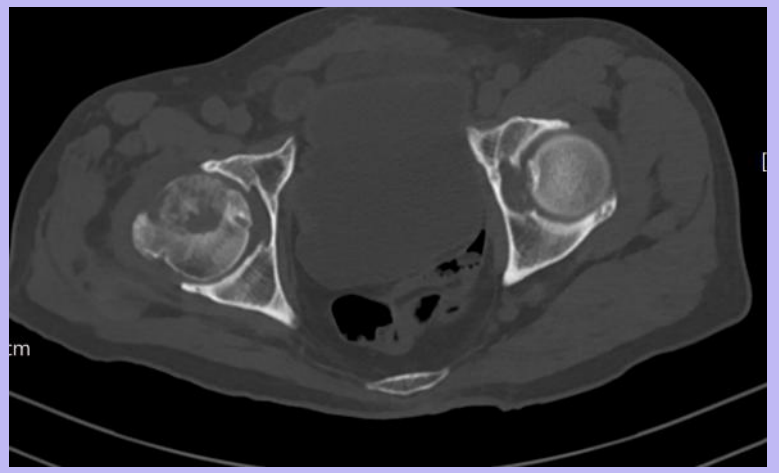
Chosen therapy
EV+P as 1L treatment

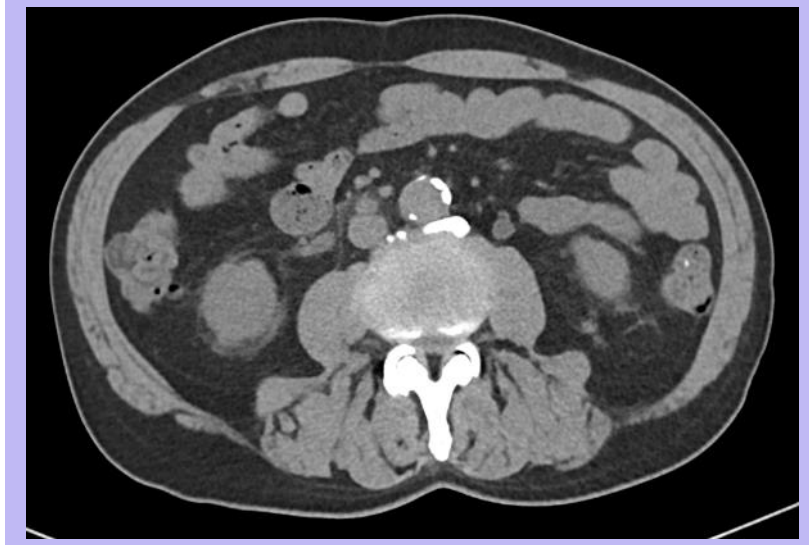
Dosing and schedule
EV 1.25 mg/kg on Day 1, 8
Pembrolizumab 200 mg Day 1 Q3W

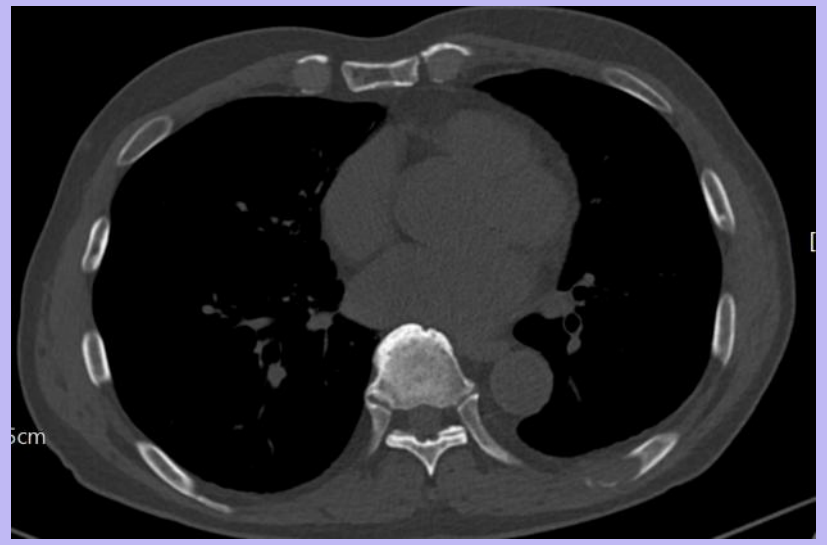
1L, first line; CT, computed tomography; EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; L1, lumbar vertebra 1; LN, lymph node; LUL, left upper lobe; Q3W, every 3 weeks

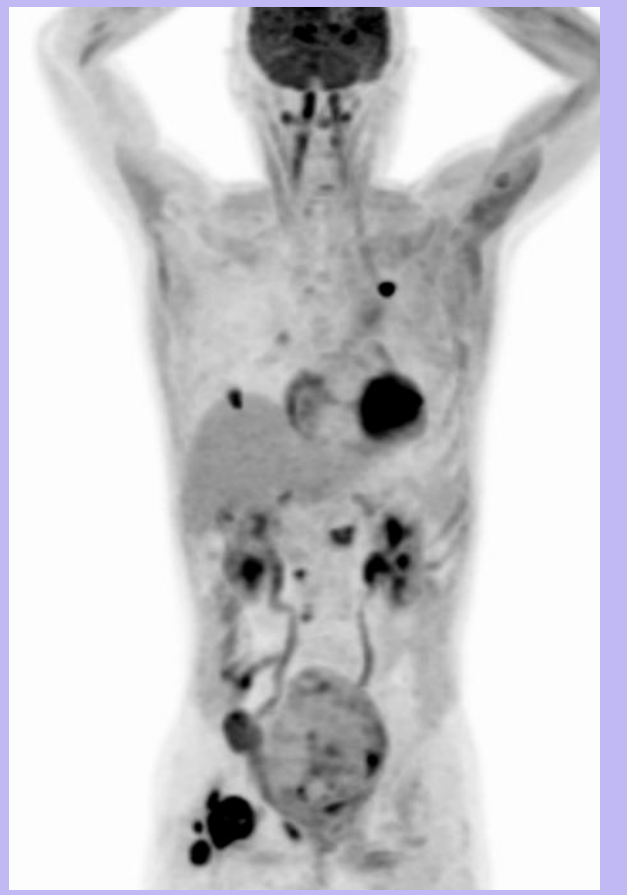
Initial patient response to treatment [1/2]











Images courtesy of Prof. Jungmin Jo with permission of the patient.

Initial patient response to treatment [2/2]

[June 2025]

Treatment
EV+P ongoing; patient tolerating well

Histopathology
Surgical pathology: INVASIVE UC(×3), HG, pT3bN0(0/18) glandular (50%) differentiation micropapillary (1%) and sarcomatoid (30%) subtypes

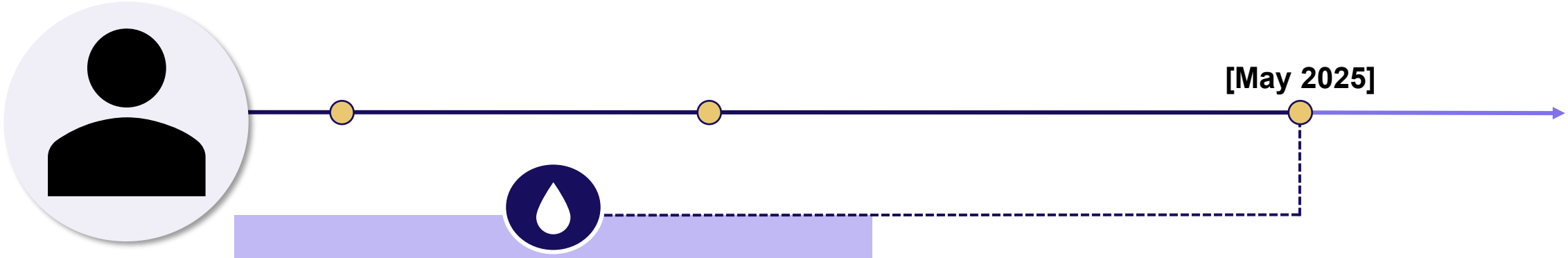
PD-L1: Positive, HER2 IHC 3+
NGS: Tier I variants; none
TMB: High (15.2 Muts/Mb)
MSS

Recovery
Pain improved after the first cycle of treatment

MDT
Continue current therapy

EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; HER, human epidermal growth factor receptor; HG, histological grade; IHC, immunohistochemistry; MDT, multidisciplinary team; MSS, microsatellite stability; Muts/Mb, mutations per megabase; NGS, next-generation sequencing; PD-L1, programmed cell death ligand 1; TMB, tumor mutational burden; UC, urothelial carcinoma.

AE presentation and management: [Hyperglycemia]



AE symptoms
Asymptomatic; detected on routine monitoring

AE assessment and grade:
Blood glucose 338 mg/dL after C1D8 (from 191 mg/dL), Grade 2
HbA1c 7.6 ← 6.7

Drug associated with AE:
EV (onset, severity)

AE, adverse event; C1D8, Cycle 1 Day 8; EV, enfortumab vedotin; HbA1c, glycated hemoglobin.

Question for the audience

Which of these statements is true?

- **A** This patient should not have been treated with EV+P as they have underlying type 2 diabetes mellitus
- **B** Administration of EV+P should be discontinued in view of Grade 2 hyperglycemia
- **C** Diabetes mellitus is a risk factor for hyperglycemia when treating patients with EV+P
- **D** In case of Grade 2 hyperglycemia, the dose of EV must be reduced

EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab.

Question for the audience

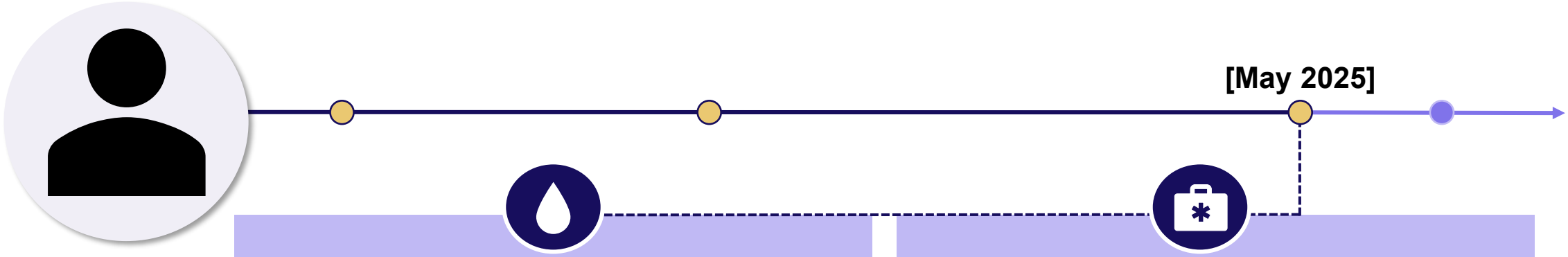
Which of these statements is true?

- **A** This patient should not have been treated with EV+P as they have underlying type 2 diabetes mellitus
- **B** Administration of EV+P should be discontinued in view of Grade 2 hyperglycemia
- **C** Diabetes mellitus is a risk factor for hyperglycemia when treating patients with EV+P[1]
- **D** In case of Grade 2 hyperglycemia, the dose of EV must be reduced

EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab.

1. Brower B et al. *Front Oncol* 2024;14:1326715.

AE presentation and management: [Hyperglycemia]



AE symptoms
Asymptomatic; detected on routine monitoring

AE assessment and grade:
Blood glucose 338 mg/dL after C1D8 (from 191 mg/dL), Grade 2
HbA1c 7.6 ← 6.7

Drug associated with AE:
EV (onset, severity)

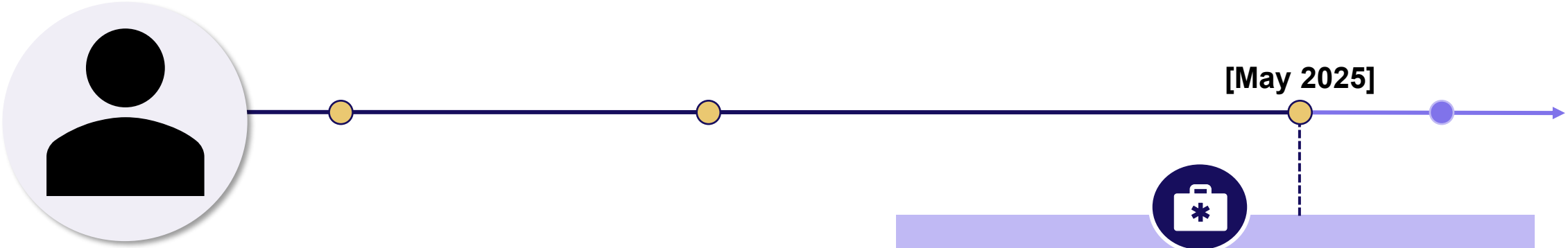
Referral to specialist
Referred to endocrinology; oral hypoglycemic agents were added

Dose interruption/reduction and duration of this:
EV+P was continued with close monitoring

Management strategies:
Metformin and gliclazide were added for glucose control

AE, adverse event; C1D8, Cycle 1 Day 8; EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; HbA1c, glycated hemoglobin.

AE management: [Hyperglycemia]



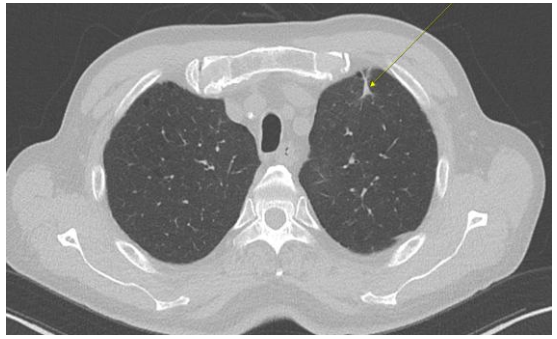
<u>Effect of AE management strategies on AE:</u>
<u>Resolved in 2 weeks; glucose well controlled</u>
Blood glucose remains controlled under 200 mg/dL without modification of EV or P

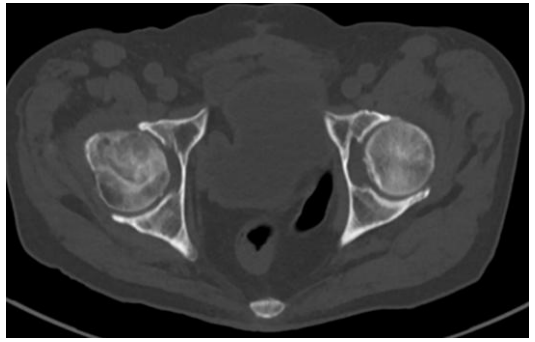
<u>Subsequent treatment:</u>
<u>Continued EV+P without further delay</u>

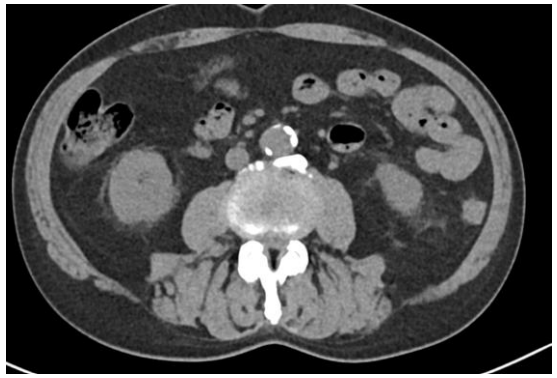
AE, adverse event; EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; P, pembrolizumab.

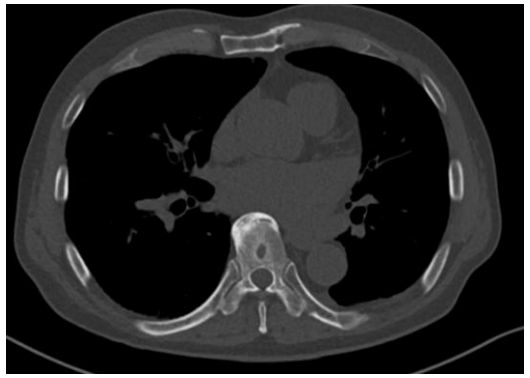
Long-term response to treatment

[June 2025]









CT scan
First response assessment scheduled for June 25

MDT
Continue current therapy with monthly glucose monitoring

Images courtesy of Prof. Jungmin Jo with permission of the patient.
CT, computed tomography; MDT, multidisciplinary team.

Eligibility criteria are restrictive and not aligned to guideline recommendations

Proposed eligibility criteria[1]

Patients who may not be optimal candidates for EV+P if they meet <u>at least two</u> of the criteria:

- Hemoglobin A1c ≥8%
- Grade ≥2 sensory or motor neuropathy
- Any corneal or retinal abnormality
- CrCl/GFR ≤45 mL/min
- ECOG PS score ≥2

EV-302 exclusion criteria[2]

Patients applicable to any of following criteria were excluded:

- Hemoglobin A1c ≥8%
- Grade ≥2 sensory or motor neuropathy
- Active keratitis or corneal ulcerations
  - Superficial punctate keratitis are allowed if the disorder is being adequately treated in the opinion of the investigator
- CrCl/GFR <30 mL/min
- ECOG PS score ≥3

- ✓ Most regimens in oncology treatment do not have criteria or guidelines
- ✓ Many of the EVITA criteria appear to be more restrictive than EV-302 in/exclusion criteria and PADCEV package insert
- ✓ Rather than focusing on strict ineligibility criteria, treatment decisions should be based on patient assessment, international guidelines, and SmPC guidance for treatment initiation with EV+P

CrCl, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; EV+P, enfortumab vedotin plus pembrolizumab; GFR, glomerular filtration rate; PS, performance status; SmPC, Summary of Product Characteristics.

1. Grande E et al. *Eur Urol* 2024:86:e152–153; 2. Powles T et al. *N Engl J Med* 2024;390:875–888 (protocol.)

It is important we understand the safety profile of EV+P to stay ahead of AESIs

Skin toxicities[1,2]

Incidence: 70%
Grade ≥3: 17%

Severe skin reactions:[1]

1.7 months

Range: 0.1–17.2 months

Peripheral neuropathy[1–3]

Incidence: 63.2%
Grade ≥3: 6.8%

Grade ≥2:[3]

6 months

Range: 0.3–25 months

EV-302 trial exclusion criteria:[4]

Ongoing sensory or motor neuropathy Grade ≥2

Hyperglycaemia[1–3]

Incidence: 13.0%
Grade ≥3: 8.9%

Any grade:[3]

0.5 months

Range: 0.3–3.5 months

EV-302 trial exclusion criteria:[4]

Uncontrolled diabetes, defined as HbA1c ≥8% or HbA1c 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained

Pneumonitis/ILD[1,2]

Incidence: 10.3%
Grade ≥3: 3.5%*

Any grade:[1]

4 months

Range: 0.3–26.2 months

EV-302 trial exclusion criteria:[4]

History of idiopathic pulmonary fibrosis, organising pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis

Ocular AEs[1–3]

Incidence: 21.4%

EV-302 trial exclusion criteria:[4]

Active keratitis or corneal ulcerations

Median time to onset

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).

*Two patients experience a fatal event of pneumonitis/ILD.[1]

AE, adverse event; AESI, adverse event of special interest; EV, enfortumab vedotin; HbA1c, glycated haemoglobin; ILD, interstitial lung disease; P, pembrolizumab.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. KEYTRUDA® (pembrolizumab). Summary of Product Characteristics; 3. Brower B et al. *Front Oncol* 2024;14:1326715;
4. Powles T et al. *N Engl J Med* 2024;390:875–888 (protocol).

EV-103 DE/A safety: The majority of the treatment-related AESIs improved or resolved in 5-year follow-up of the previous study

Onset, improvement, and resolution for treatment-related AESIs for EV

	Total number of events* n	Events* with improvement n(%)	Events* with resolution n(%)	Median time to:		
				Onset of first event (range), mo	Improvement† (range), mo	Resolution‡ (range), mo
Skin reaction	66	2 (3.0)	59 (89.4)	0.7 (0.1–15.7)	0.7 (0.2–1.2)	1.2 (0.1–27.1)
Peripheral neuropathy	43	19 (44.2)	11 (25.6)	2.4 (0.7–12.5)	5.5 (0.3–27.4)	8.6 (3.5–56.7)
Hyperglycemia	7	1 (14.3)	6 (85.7)	0.5 (0.3–3.5)	0.5 (0.5–0.5)	1.6 (0.5–19.7)

- Median time to onset of skin reactions and hyperglycemia was 0.7 and 0.5 months, respectively, and median time to resolution was 1.2 and 1.6 months, respectively
- Median time to onset of peripheral neuropathy was 2.4 months, while median time to resolution was 8.6 months

*Patients could have had >1 event; †Improvement defined as at least 1 grade improvement from the worst grade at the last assessment; ‡Resolution defined as a return to baseline grade or better at the last assessment or recovered outcome.
AESI, adverse event of special interest; DE/A, dose escalation/Cohort A; EV, enfortumab vedotin; mo, months.
Rosenberg JE et al. Presented at ESMO 2024. 1968P.

Hyperglycemia: Risk factors and monitoring

Median time to onset of hyperglycemia:[1]
0.5 months

Hyperglycemia is an AESI associated with EV+P that occurs infrequently but can become severe or fatal[1]

General risk factors[1]

- Prior diabetes mellitus
- Increased BMI
- Illness/infection
- Use of systemic steroids
- Underlying fatty liver disease

Before initiation of EV (baseline)

Screen for signs of diabetes or hyperglycemia[2]*

Before each EV dose

Assess blood glucose prior to dosing[2]

Between EV doses

Conduct periodic monitoring of blood glucose throughout course of treatment[2]

Glucose-raising medications

Medications may increase blood glucose levels (including steroids used to treat other AESIs). Close monitoring may be required in these patients[1]

Specialist referral

If there is concern for ongoing poor glucose control (e.g., >250 mg/dL) consider referral to an endocrinologist[1]

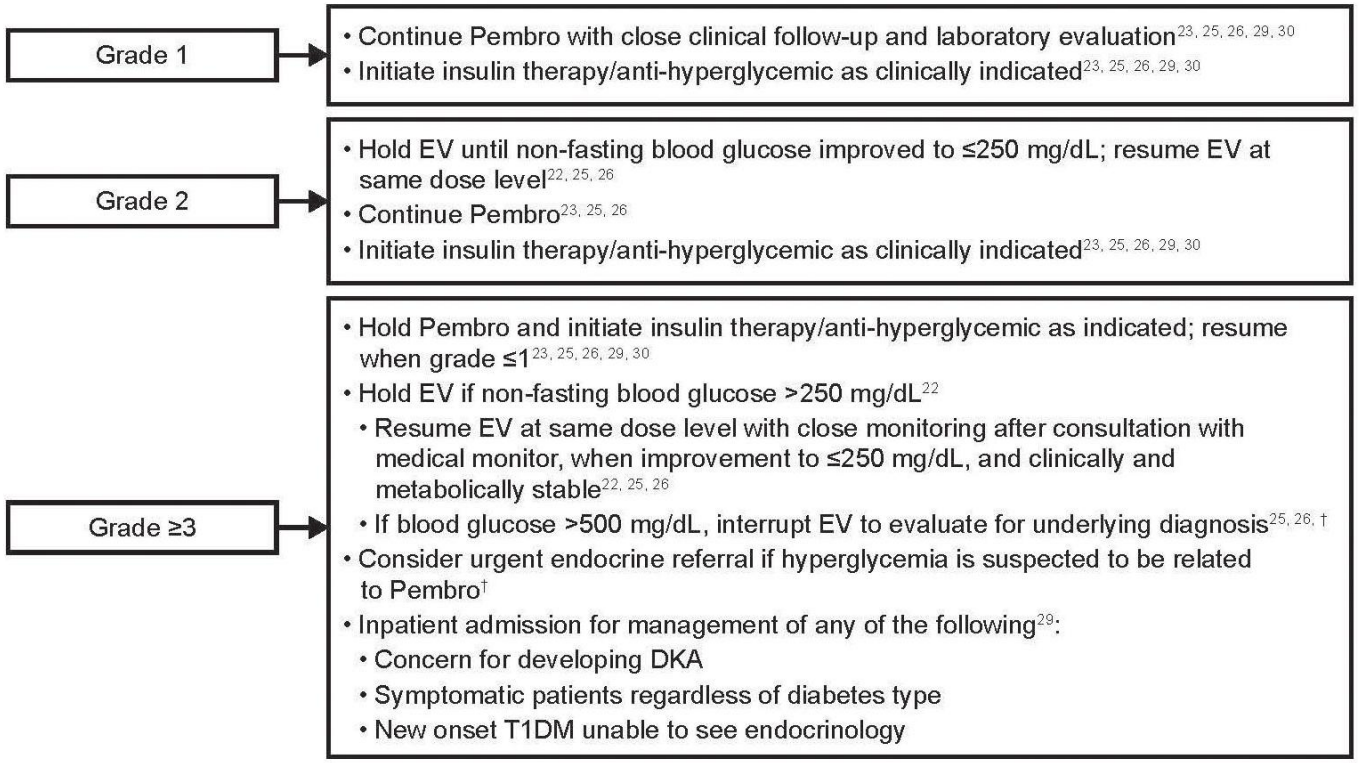
*Hyperglycemia occurred more frequently in patients with baseline hyperglycemia or BMI ≥30 kg/m^2. Patients with baseline HbA1c ≥8% were excluded from clinical trials.[2]
AESI, adverse event of special interest; BMI, body mass index; EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; HbA1c, glycated hemoglobin.
1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

There is established guidance in the SmPC to help manage hyperglycemia

AESI	SmPC management guidance
Hyperglycaemia	If **blood glucose is elevated** >13.9 mmol/L (>250 mg/dL), **EV should be withheld** until blood glucose is ≤13.9 mmol/L • **Resume** at the **same dose level**

AESI, adverse event of special interest; EV, enfortumab vedotin; SmPC, Summary of Product Characteristics.
PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

Hyperglycemia: Management[1]



If evidence of DKA:[1]
- Hold P until DKA resolves
- Endocrine referral
- Inpatient management
- Manage DKA per guidelines
- Initiate insulin as clinically indicated

Images reproduced from 'Managing potential adverse events during treatment with enfortumab vedotin + pembrolizumab in patients with advanced urothelial cancer' Brower B et al. Front Oncol 2024;14:1326715. Available at: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2024.1326715/full. By CC: https://creativecommons.org/licenses/by-nc/4.0/.
DKA, diabetic ketoacidosis; EV, enfortumab vedotin; P, pembrolizumab; T1DM, type 1 diabetes mellitus.
1. Brower B et al. *Front Oncol* 2024;14:1326715.

Summary

Early hyperglycemia (onset 0.5 months) highlights the need for close monitoring during initial cycles of EV+P treatment, enabling early intervention[1]

When hyperglycemia is manageable, treatment discontinuation is not necessarily required. Early intervention provides the best chance of resolution ensuring patients can continue to receive their treatment[1,2]

EV+P is an effective treatment option for a broad patient population including those with comorbidities and difficult-to-treat cases. Effective management strategies can be utilized to manage hyperglycemia/diabetes mellitus to ensure patients are able to receive optimal treatment outcomes[1,2]

EV, enfortumab vedotin; P, pembrolizumab.

1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

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Please refer to the Korean PI for PADCEV® (enfortumab vedotin) via the following link or QR Code:

<PADCEV 20mg>

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PI, Prescribing Information

Genitourinary Masterclass

Best-practice sharing: Practical approaches to patient care – Part 1

Dr. Jiun-I Lai

Division of Medical Oncology, Department of Oncology,
Veterans General Hospital, Taipei, Taiwan

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EV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 or programmed death-ligand 1 inhibitor and have received a platinum-containing chemotherapy.

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July 2025: MAT-KR-PAD-2025-00073

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Speaker disclosures

- I have no disclosures relevant to this presentation

Case 1
Introducing – Ms. Cheng

Ms. Cheng

- Taiwanese female
- **Age: 65** years
- **ECOG PS: 1**
- **GFR: 45** mL/min
- **BMI: 13.7** kg/m^2

Lifestyle: Light activity

Employment status/job: Hotel owner

Family history of cancer: None

Comorbidities: None

Concomitant medications: None

Any other relevant medical history: None

Habits:

Priorities:

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate.

Diagnosis (1/3)

Initial presentation

- Palpitation and dizziness; came to our ER
- Blood check: Hb 5.7 g/dL; tarry stool noted

Further investigations

UGIPES was done: one 5 cm tumor mass with easy contact bleeding noted over the periampullary region at the second portion

Pathology:

The biopsy shows duodenal mucosa with infiltrative carcinoma cells in solid and papillary architecture. The carcinoma cells are immunoreactive for GATA3, p40, and cytokeratin and negative for INSM1 and synaptophysin. The Ki-67 labeled index is high. The pathological findings are compatible with metastatic carcinoma and urothelial origin is the most likely origin

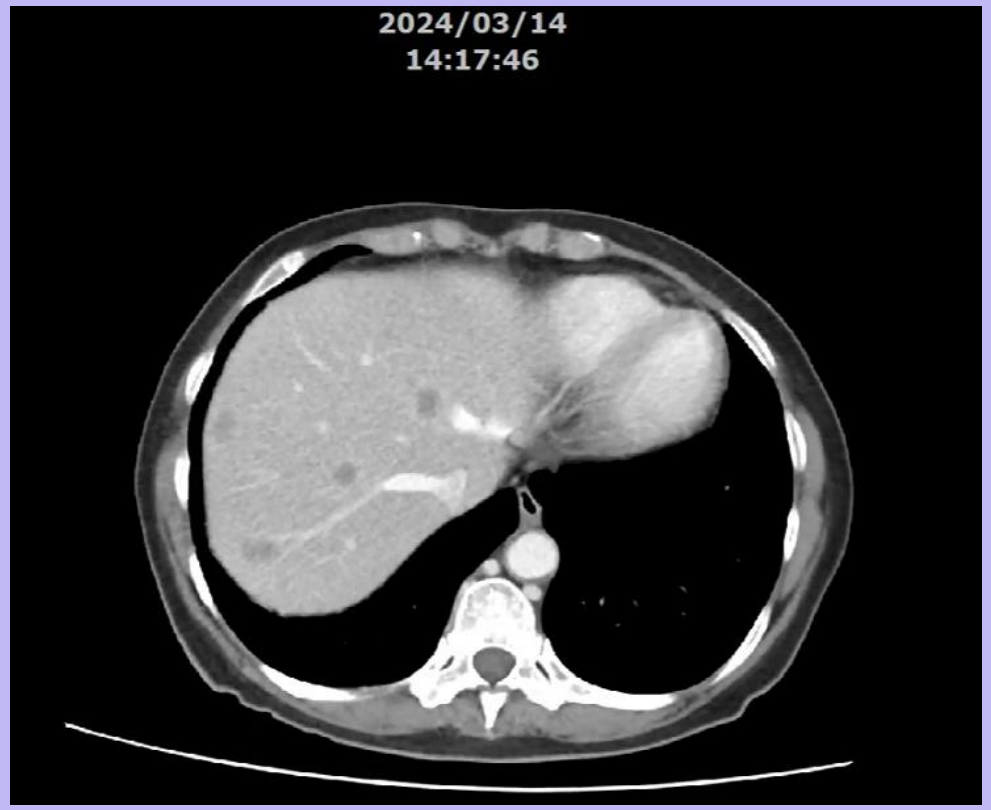
Diagnosis (2/3)

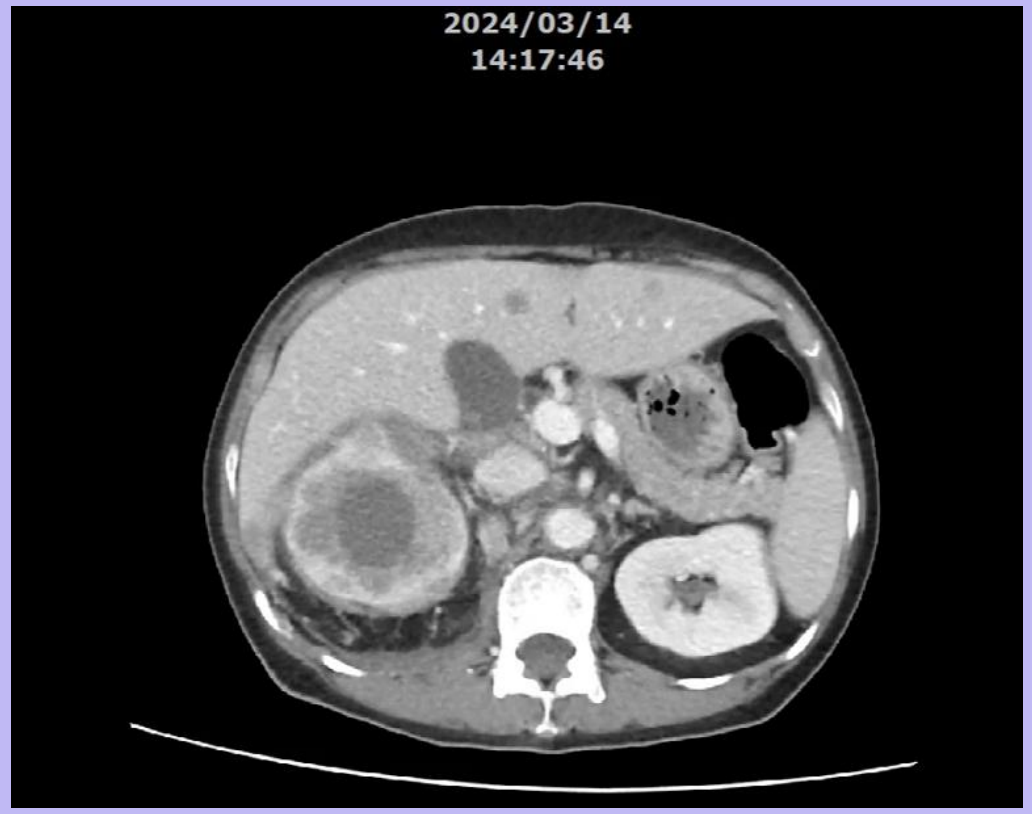
Imaging

- Abdominal CT:
  - Right renal tumor with vascular involvement, LAP, right ureter involvement
  - Suspected LAP encasement or tumor involving left ureter
  - Bilateral hydroureter, left hydronephrosis
  - Lung and liver mets
  - R/O mass at superior wall of urinary bladder

CT, computed tomography; LAP, laparoscopic; mets, metastases; R/O, radiologically observed.

Initial patient response to treatment





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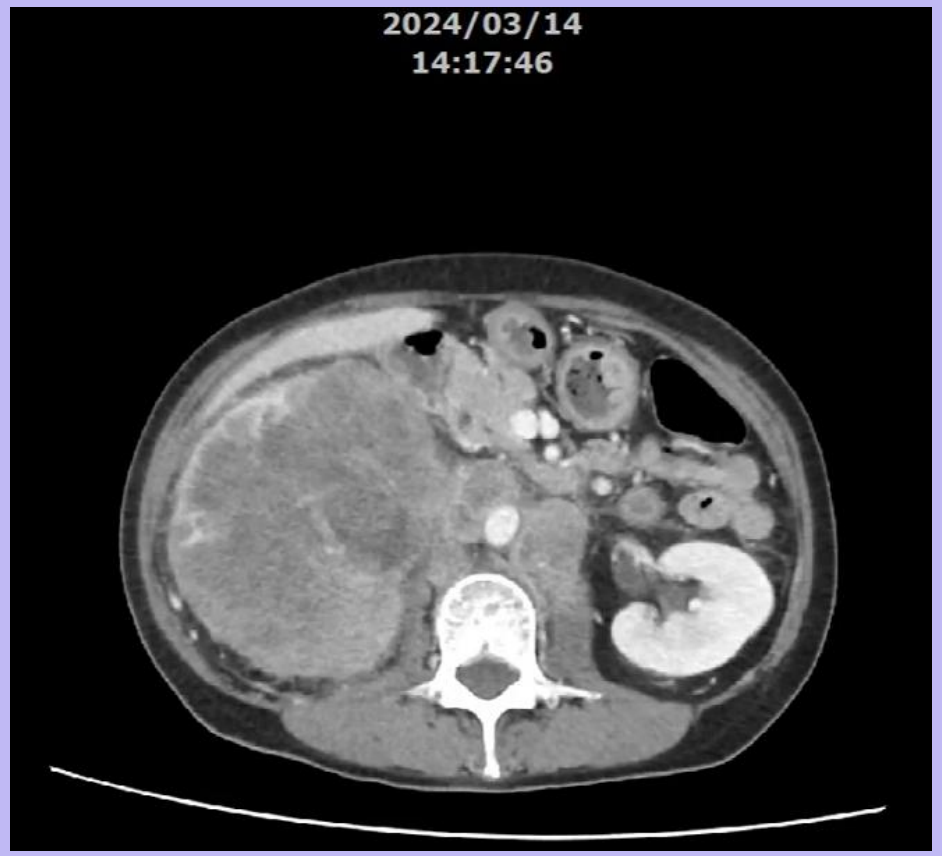
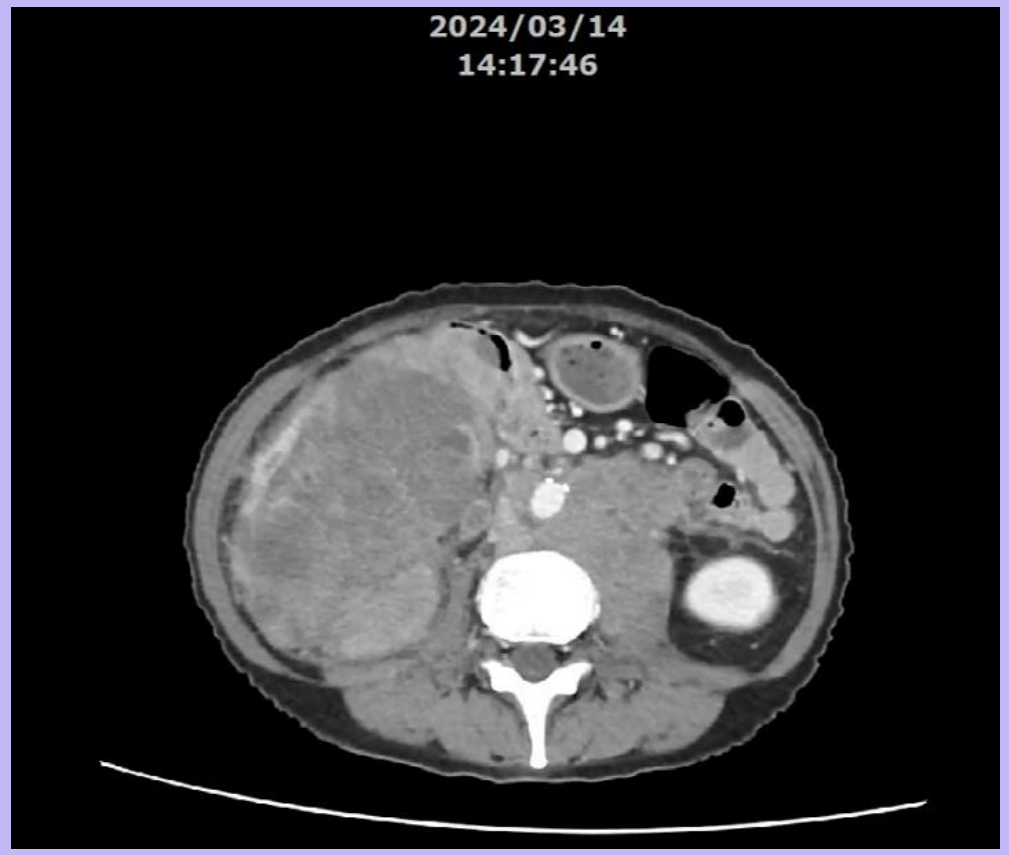
Initial patient response to treatment





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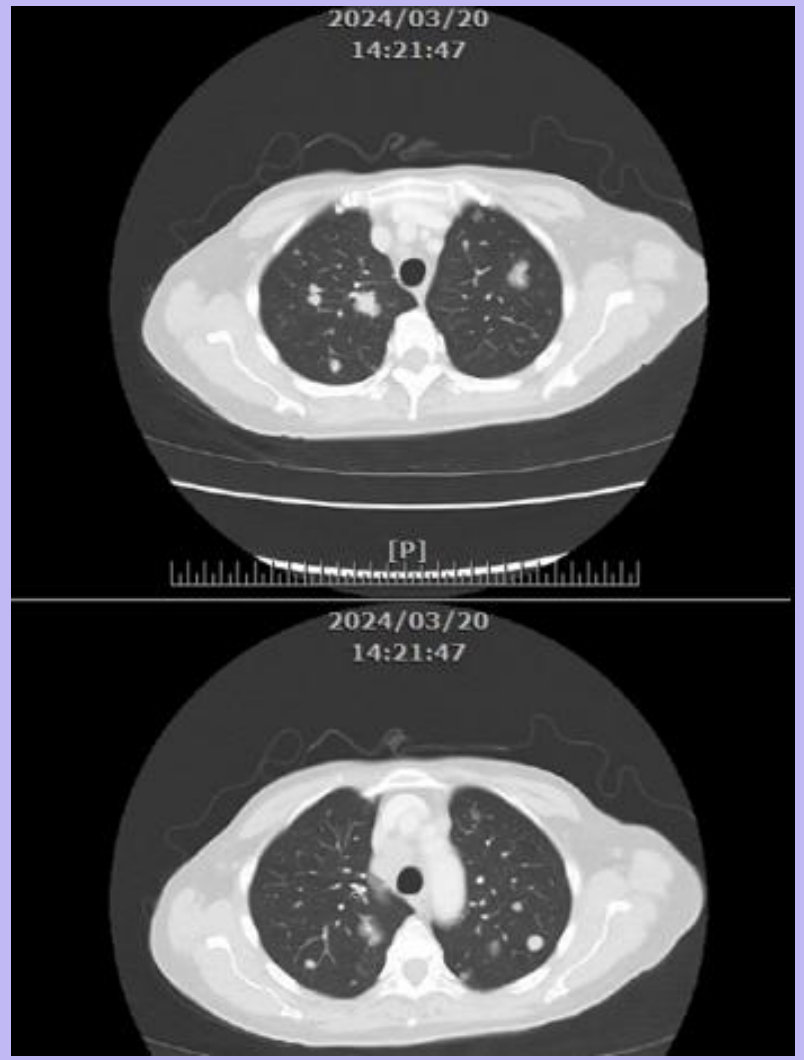
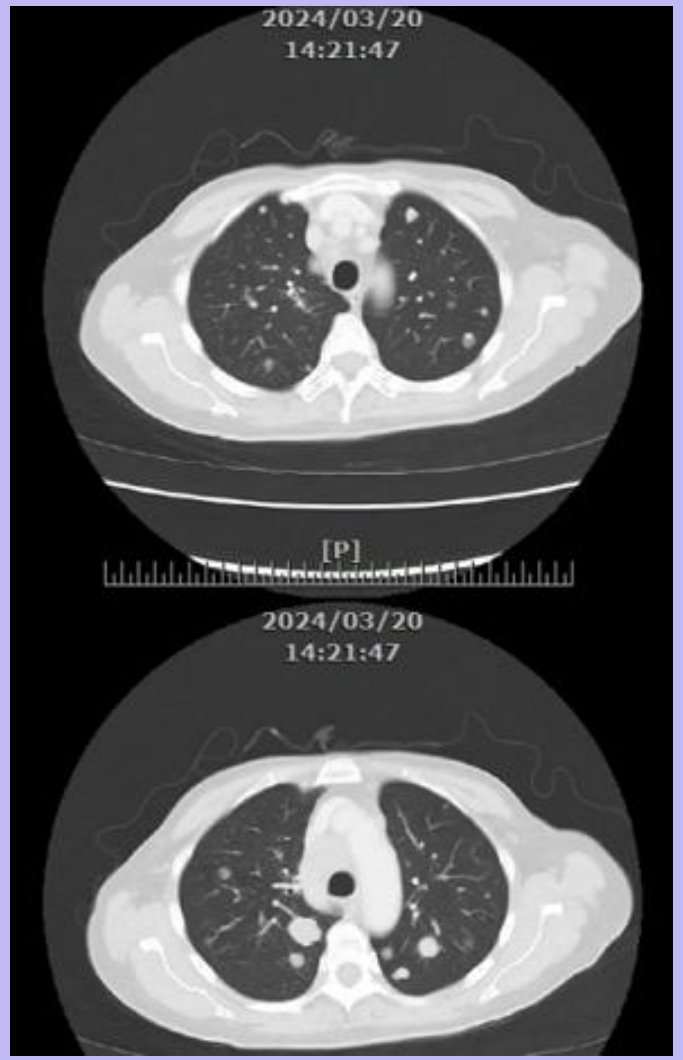
Initial patient response to treatment





Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Diagnosis (3/3)

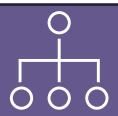
- Right renal pelvis urothelial carcinoma with **ureter** and **bladder** involvement, with **lung, liver, and abdominal lymphadenopathy metastases, direct invasion to duodenum with intestinal bleeding**, with hydronephrosis, hydroureter, T4N2M1

UTUC clinical features and prevalence

UTUC is uncommon, accounting for only 5–10% of all urothelial carcinomas[1]

In Taiwan, the incidence is relatively high and is associated with endemic “blackfoot disease,” due to arsenic exposure[2]

UTUC is considered aggressive and is associated with female sex, high T stage, and end-stage kidney disease[1,2]



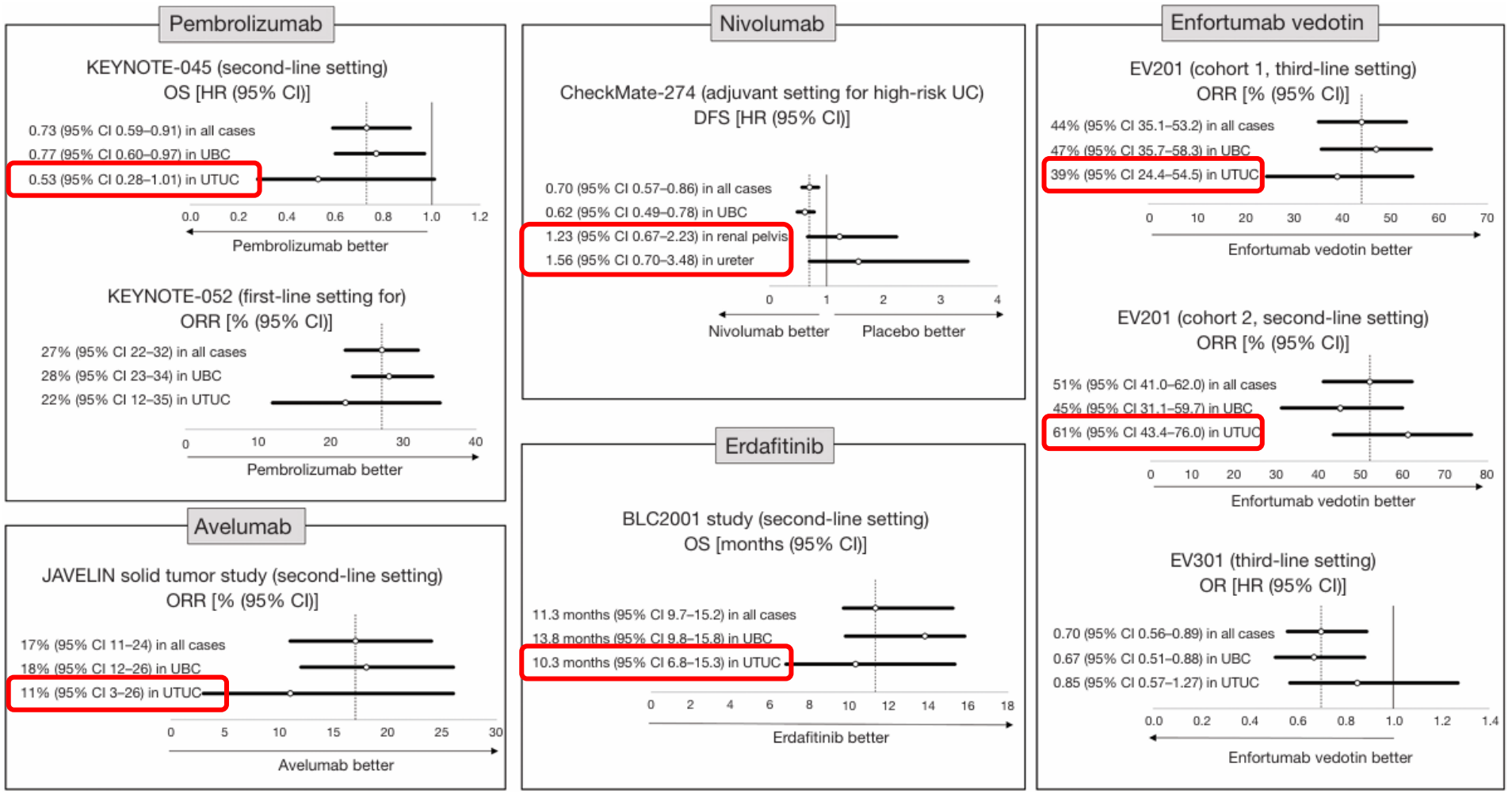
Increasing evidence suggests that clinical and biological features are distinct for UTUC vs. LTUC[1]

UTUC seems to present more frequently with high histologic grade, advanced clinical stage, and metastasis accompanied by worse prognosis compared with UBC[1,2]

LTUC, lower urinary tract urothelial carcinoma; UBC, urothelial bladder carcinoma; UTUC, upper urinary tract urothelial carcinoma.

1. Roupret M, et al. Eur Urol 2011;59:584-94; 2. Lin M-Y, et al. Int J Urol 2022;29:121-127.

Metastatic UTUC is associated with poor outcomes



Studies are shown for illustrative purposes and should not be directly compared. Images reproduced from 'Comparison of molecular profiles of upper tract urothelial carcinoma vs. urinary bladder cancer in the era of targeted therapy: a narrative review. Available at: https://tau.amegroups.org/article/view/105993/html. By CC: https://creativecommons.org/licenses/by-nc/4.0/

CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; OR, overall response; ORR, overall response rate; OS, overall survival; UBC, urinary bladder carcinoma; UC, urothelial carcinoma; UTUC, upper urinary tract urothelial carcinoma.

Tomiyama E et al. *Transl Androl Urol* 2022;11:1747–1761.

UC with either direct invasion or metastases to GI tract is rare and usually associated with poor outcomes (3–15 months OS)

Author (Year)	Age/Sex	Pathology	IHC Positive/Negative	Biopsy approach	Symptoms	Rectal tumor extension
Langenstroer P et al. (1996)	73/M	TCC PD/focal adenocarcinoma and signet ring cell	NO	Needle	Fatigue, weight loss, chronic diarrhea, rectal pain	DISTAL R
Ha HK et al. (2000)	N/S	TCC	NO	NS	NS	NS
Hong SP et al. (2002)	63/M	TCC papillary	NO	Colonoscopy	Jaundice, constipation, weight loss	NS
Yusuf TE et al. (2005)	54/M	TCC G3	NO	Mucosal biopsy negative, EUS-FNA AND EUS-TCB	Change in bowel habits	DISTAL R
Yusuf TE et al. (2005)	73/M	TCC PD	NO	Mucosal biopsy negative, EUS-FNA	Severe constipation	DISTAL R
Gleeson FC et al. (2008)	54/M	TCC/G3	CK 7, CK 20	EUS-FNA AND EUS-TCB	Presumed refractory ulcerative proctitis	DISTAL MEDIUM R
Gleeson FC et al. (2008)	55/M	TCC/G3	CK 7, CK 20	EUS FNA AND EUS TCB	Altered bowel habit (constipation)	ALL RECTUM
Gleeson FC et al. (2008)	60/M	TCC/G3	CK7, CK 20	EUS FNA	Altered bowel habit (constipation)	RECTUM
Ying-Yue J et al. (2010)	83/M	UCC PD	CK 7, CK 20/CDX-2 SI S-100	Rectoscopy	Frequent bowel movements, weight loss	DISTAL R
Katsinelos P et al. (2012)	68/M	TCC G3 papillary	CK7, CK 20/PSA	Multiple biopsies and FNA negative	Anal outlet obstruction, constipation, tenesmus	DISTAL R
Yang M-H et al. (2012)	61/M	UCC PD	CEA, CK 7, CK 20/PSA, SYNAPTOPHYSIN	Colonoscopy	Difficult defecation, abdominal distension	DISTAL R
Kassam et al. (2013)	53/M	TCC PD	CK 7, CK20	Colonoscopy	Anorexia, diffuse abdominal pain, pencil thin stools	RECTOSIGMOID
Asfour R et al. (2014)	54/M	UCC	NO	Colonoscopy	Constipation, anorexia, pain with defecation, abdominal distension	DISTAL R
Hashash JG et al. (2015)	55/M	UCC	KI 67, P 53, GATA 3	Rectal tunnel biopsies	Rectal pain, urgency, heaviness, thinning stool	DISTAL MEDIUM R
Ma Y et al. (2015)	65/M	UCC PD	P53, CK 34, CK7	Colonoscopy	Increasing constipation, faecal incontinence and tenesmus	DISTAL R
Esfandiari et al. (2016)	84/F	UCC papillary G3	CK 7, EMA, P40, GATA3, CA 125/equivocal BerEP4	Sigmoidoscopy TCB	Rectal pain on defecation, suprapubic pain, fecal and urinary incontinence	MEDIUM R
Chung Sang TSE et al. (2020)	85/M	UCC	CK 7, CK 20, GATA3	Sigmoidoscopy	Scrotal pain and swelling, hematochezia	RECTUM
Andreea de Cino et al. (2021)	81/M	UCC	NO	Sigmoidoscopy	Subacute epigastric pain, chronic constipation	NS
Li Y et al. (2021)	72/F	UCC G2	CK 7, CK 20, GATA3/CDX2	Colonoscopy	Abdominal bloating and obstructed defecation	DISTAL MEDIUM R
Nazar et al. (2022)	72/F	UCC PD	GATA3, CK20/TTF1, CDX, P63, PAX 8	Colonoscopy	Hematochezia, tenesmus, rectal pain	UPPER R
Nagahisa C et al. (2023)	67/M	UCC	GATA3/CDX 2	Colonoscopy	Severe constipation, anal pain	DISTAL R
Yang et al. (2023)	64/M	UCC	KI 67, P53, CK, GATA3, CK7	Colonoscopy, multiple rectal, finally EUS-FNAdiagnostic	Increased frequency of defecation, decrease stool volume	DISTAL MEDIUM R
Alnasarat A et al. (2024)	85/M	UCC plasmacytoid, signet ring	GATA, CK 7, CK 20/CDX	Sigmoidoscopy	Weight loss, epigastric discomfort, abdominal distension	RECTUM
Menon R et al. (2024)	75/M	UCC	P63, GATA3	Sigmoidoscopy	Rectal bleeding	DISTAL R
Present Case (2025)	64/M	UCC G3/conventional and signet ring cell	GATA3, CK 20/CK5/6, P63, CDX	Colonoscopy, rectal EUS TCB	Rectal tenesmus, transit disorders (constipation/small volume diarrhea), moderate dysuria	DISTAL MEDIUM R

Question for the audience

Considering patient history and international guidelines, what treatment approach would you favor for this patient?

- A EV monotherapy
- B Single-agent chemotherapy
- C EV+P
- D Other

Footnotes

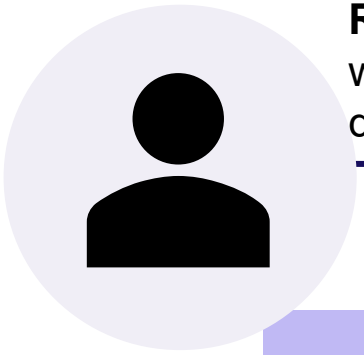
Question for the audience

Considering patient history and international guidelines, what treatment approach would you favor for this patient?

- A **EV monotherapy**
- B **Single-agent chemotherapy**
- C **EV+P**
- D **Other**

Treatment initiation, dosage, and schedule

Right renal pelvis urothelial carcinoma with ureter and bladder involvement, with lung, liver, and abdominal lymphadenopathy metastases, direct invasion to duodenum with intestinal bleeding, with hydronephrosis, hydroureter, T4N2M1



Initial presentation

Duodenal bleeding due to tumor invasion

Further investigations

Lung, liver, and abdomen metastases

Chosen therapy

EV+P

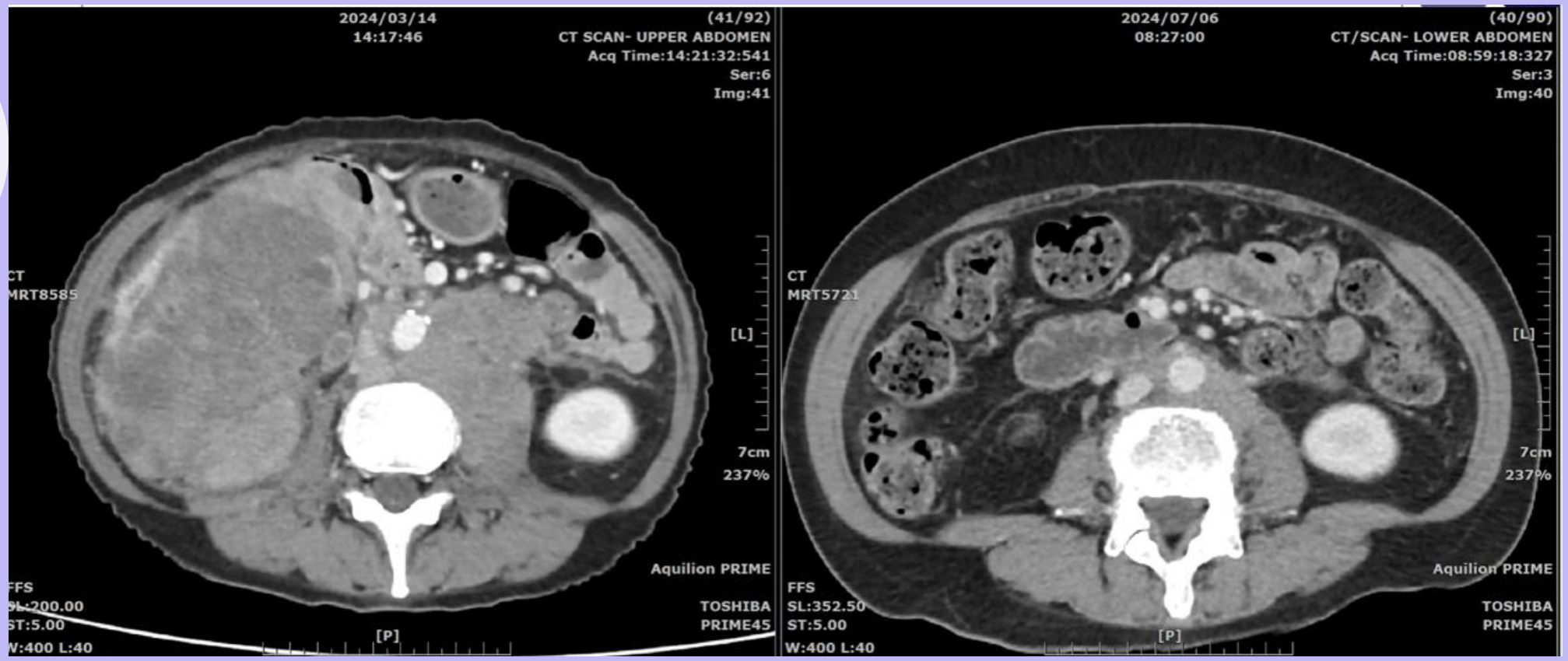
Dosing & schedule

Day 1:
Pembrolizumab
200 mg + EV 60 mg*
Day 8:
EV 60 mg*

21-day cycles

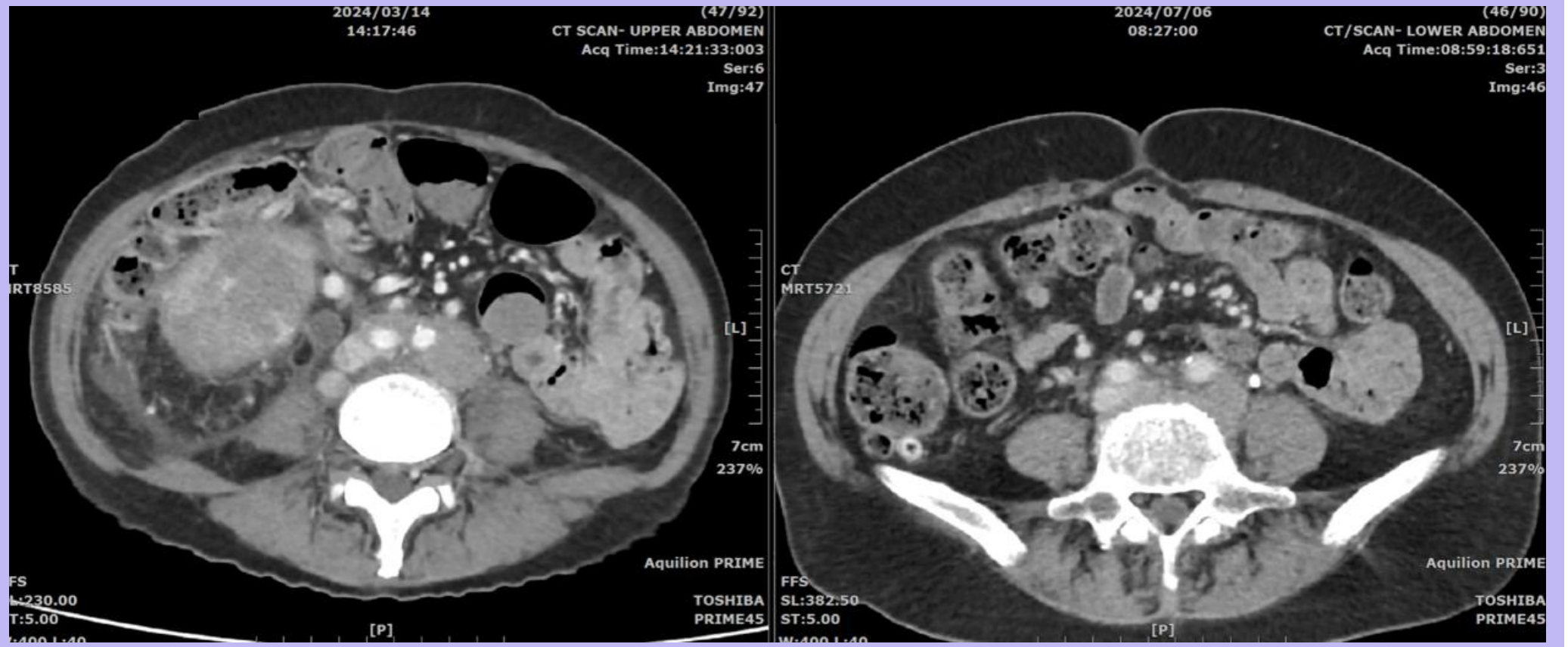
***Disclaimer: Treatment with EV should always be initiated at the recommended dosage. Always refer to local guidance.**
EV, enfortumab vedotin; P, pembrolizumab.

Treatment response



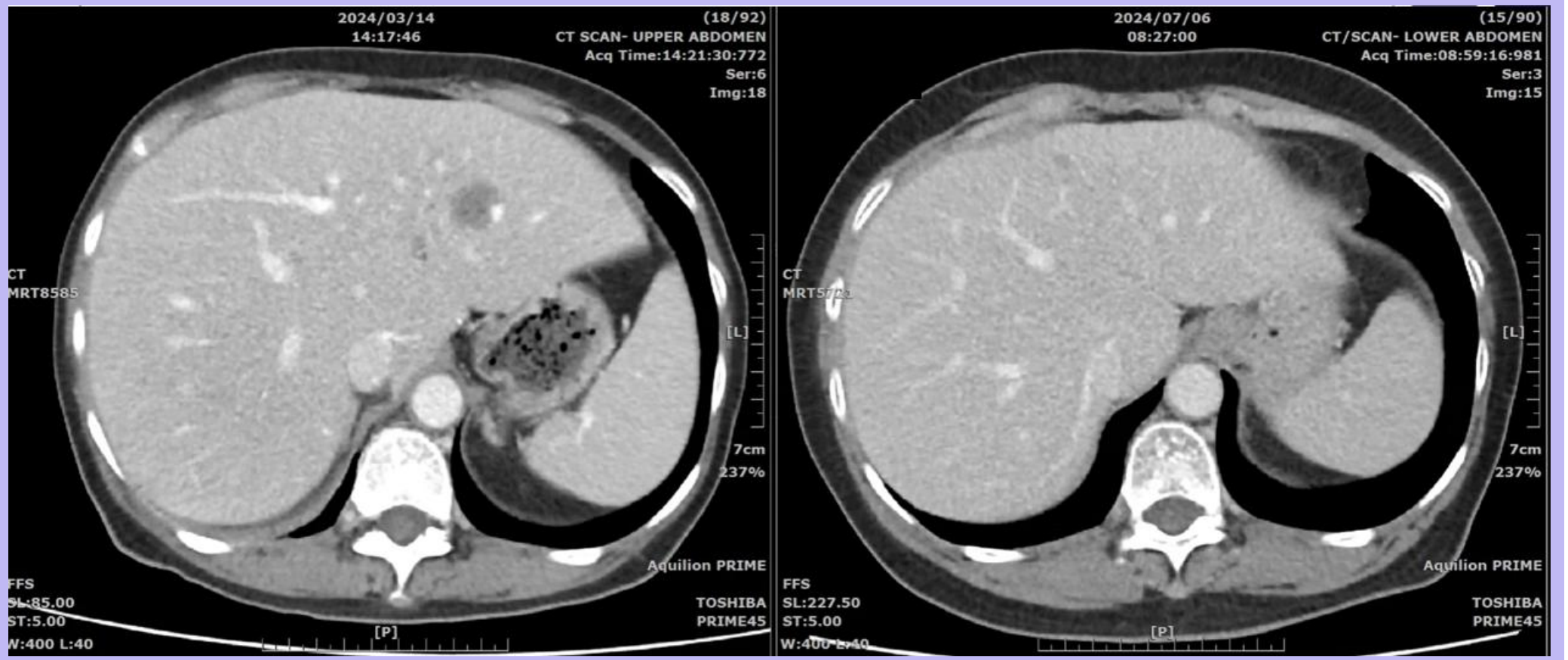
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



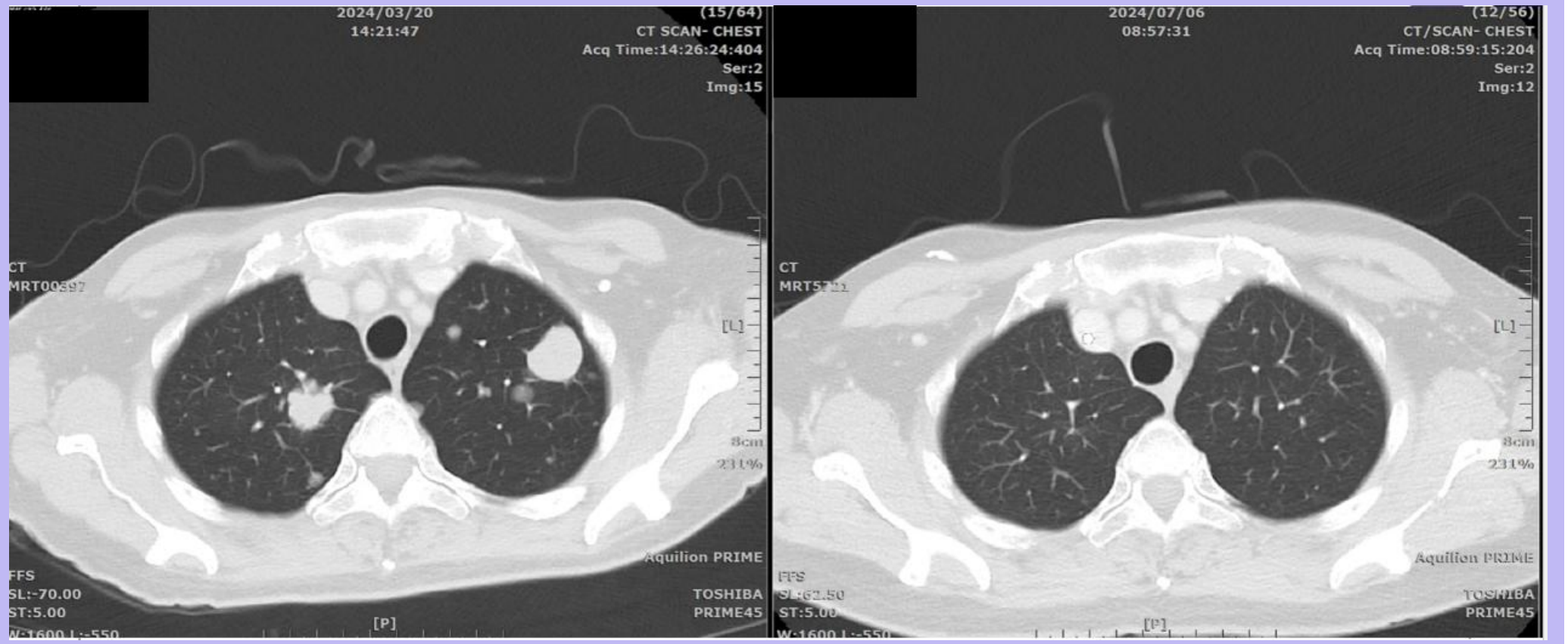
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



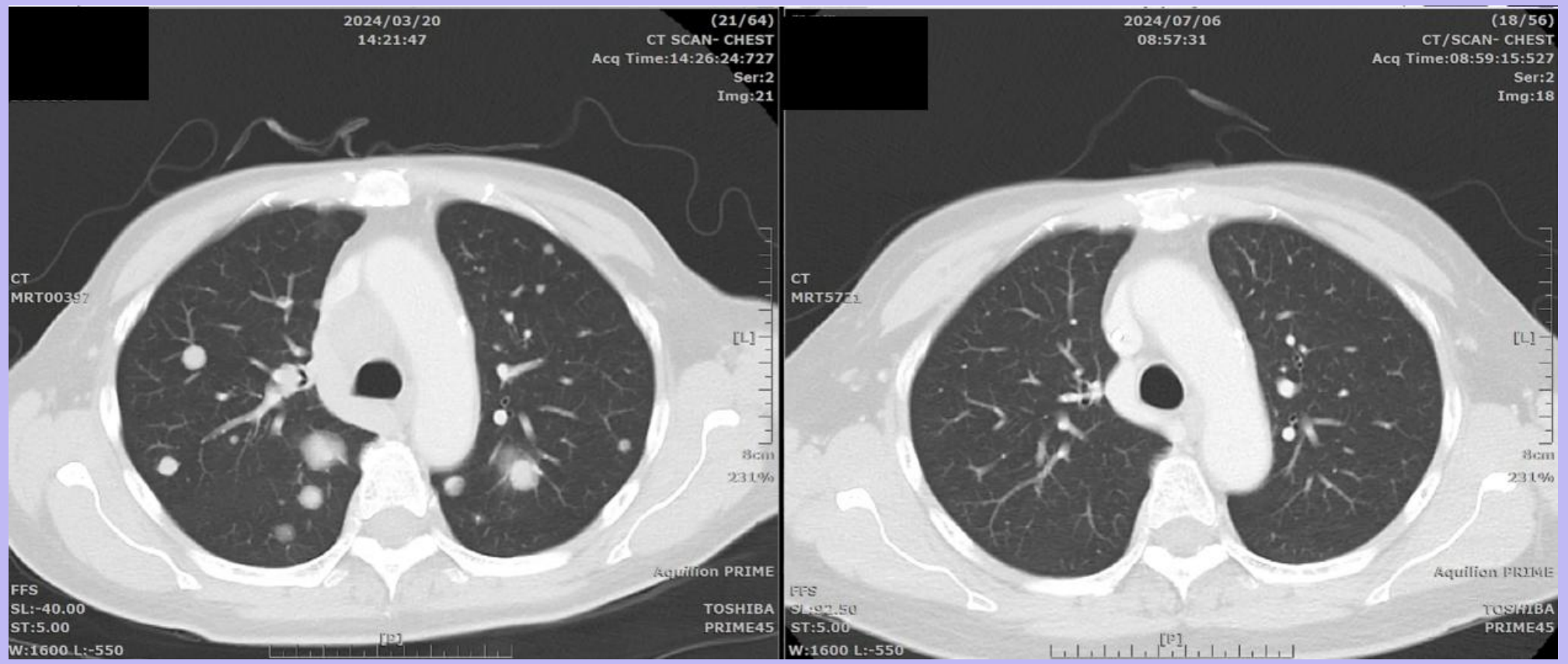
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



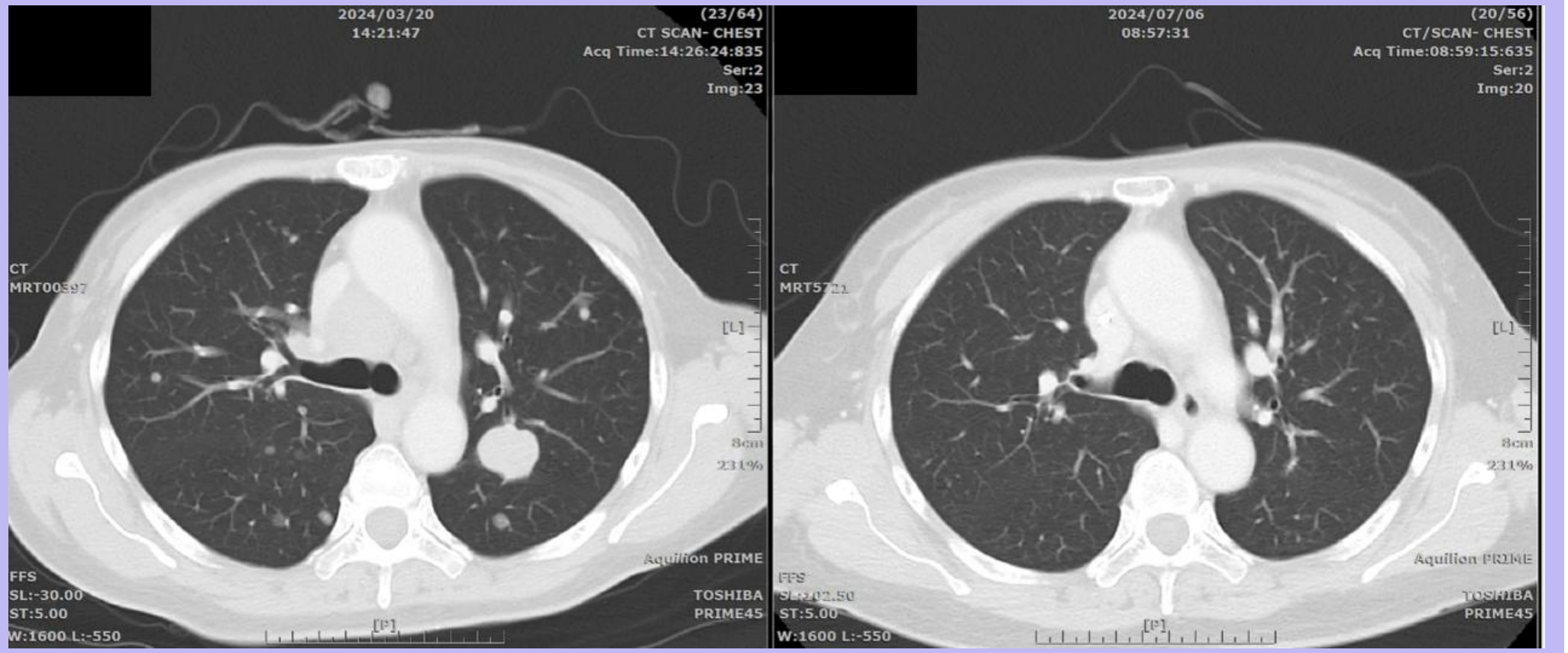
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



Images courtesy of Dr. Jiun-I Lai with permission of the patient.

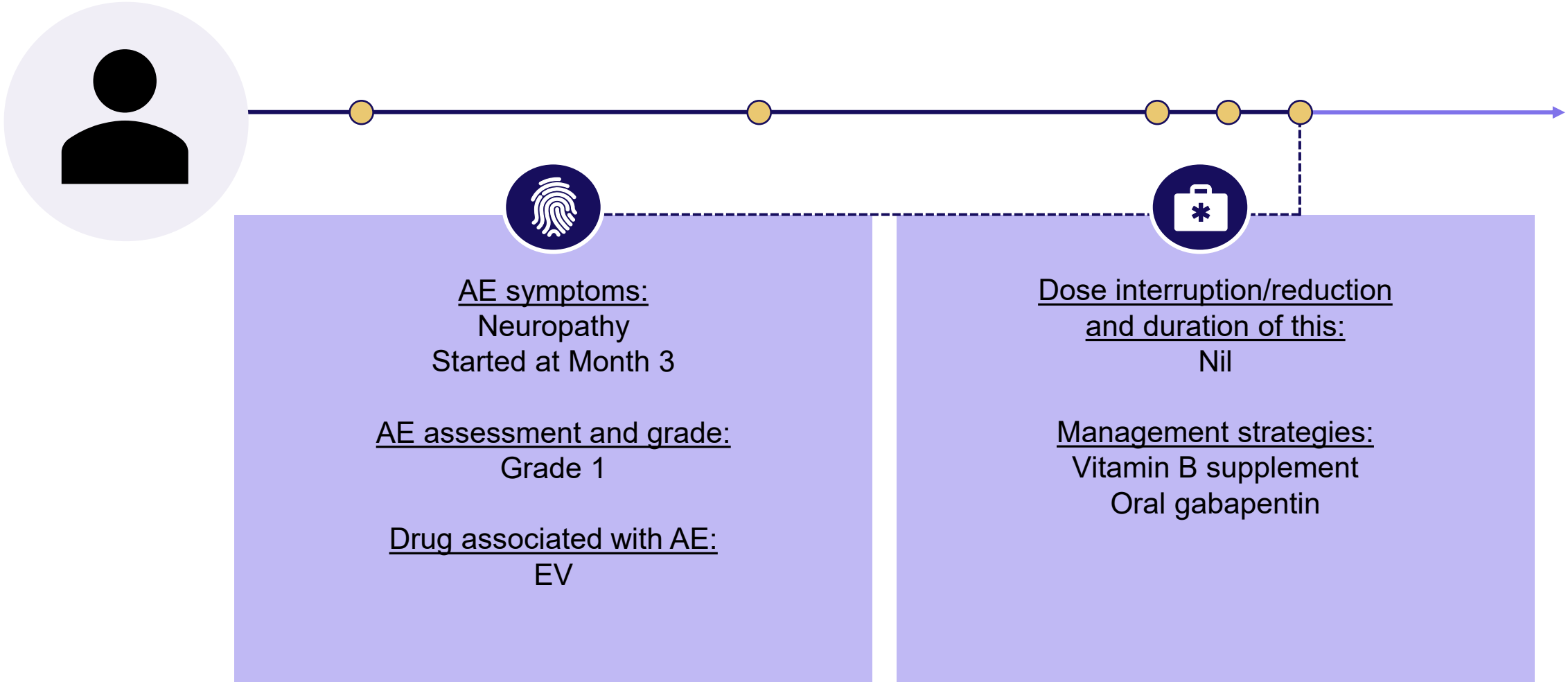
Treatment

- Right renal pelvis urothelial carcinoma with ureter and bladder involvement, with lung, liver, and abdominal lymphadenopathy metastases, direct invasion to duodenum with intestinal bleeding, with hydronephrosis, hydroureter, T4N2M1
- Started on EV+P as first-line treatment
- Restaging in 3 months:
  Near CR in lung and liver metastases
  Significant regression of main tumor, at least PR
- Patient well, with excellent quality of life

Fictitious patient case study created for illustrative purposes.

CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PR, partial response.

AE presentation and management



AE, adverse event; EV, enfortumab vedotin.

Neuropathy can be graded according to the CTCAE

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Peripheral motor neuropathy	Asymptomatic; clinical or diagnostic observations only	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	N/A
Peripheral sensory neuropathy	Asymptomatic	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	N/A
Neuralgia	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL	N/A	N/A

ADLs, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events.

US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Available at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Last accessed: June 2025.

Case summary

De novo UTUC with lung, liver, and lymphadenopathy involvement, with invasion to duodenum and intestinal bleeding

Good response to first-line EV+P treatment

EV+P was generally well tolerated, with the patient experiencing Grade 1 neuropathy that did not require a treatment interruption

EV, enfortumab vedotin; P, pembrolizumab; UTUC, upper urinary tract urothelial carcinoma.

Case 2 Introducing – Ms C

Ms C

- Taiwanese female
- **Age:** 72 y/o
- **ECOG PS: 0**
- **GFR: 90** ml/min
- **BMI: 20.7** kg/m^2

Lifestyle: Light activity
Employment status/job: Retired
Family history of cancer: None

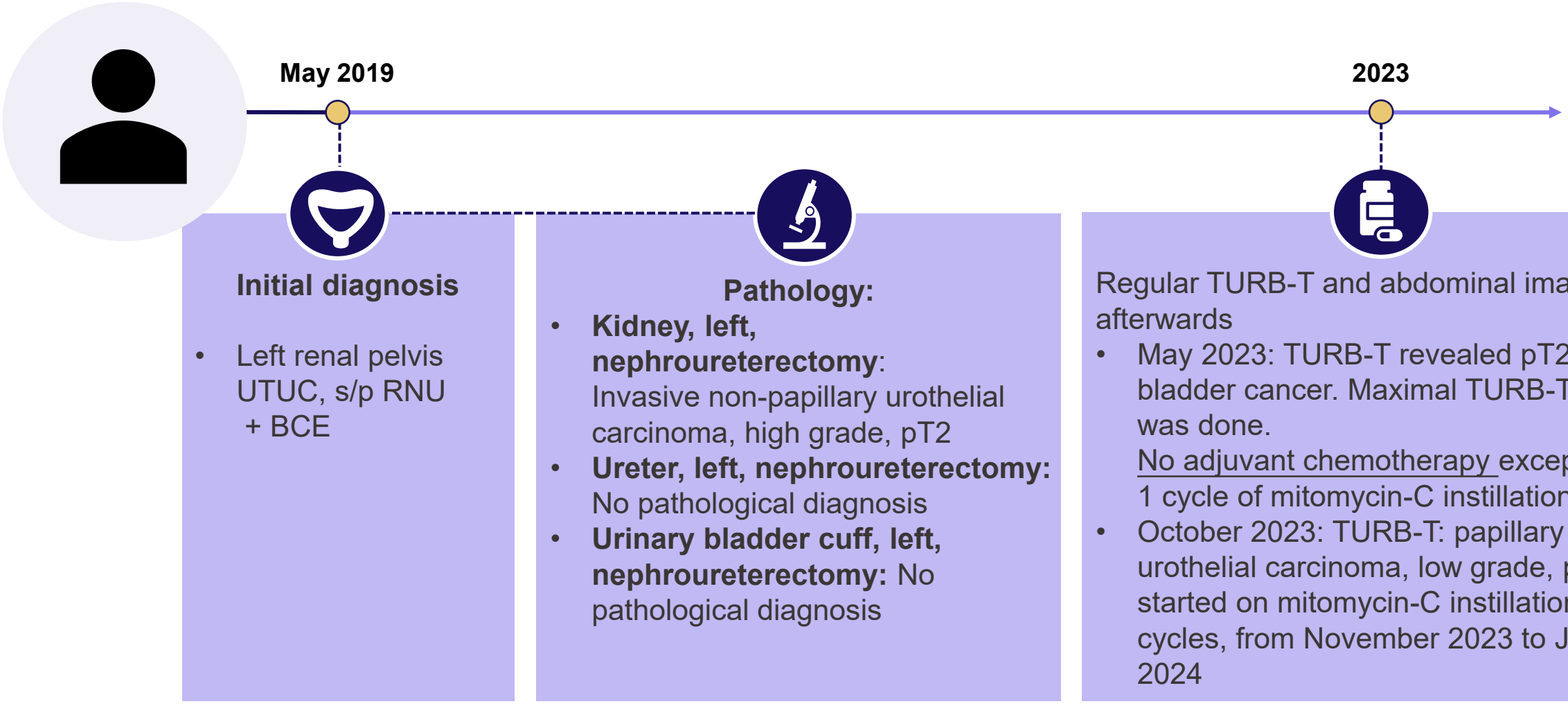
Comorbidities: HTN
Concomitant medications: None
Any other relevant medical history:
Left renal pelvis invasive non-papillary UC, high grade, pT2N0M0

- s/p left diagnostic ureterorenoscopy and biopsy on 2019/05/08 (Pathology: papillary urothelial carcinoma, low grade)
- s/p laparoscopic left radical nephroureterectomy + bladder cuff excision on 2019/05/23

Habits: none

HTN, hypertension; s/p, status post; UC, urothelial carcinoma.

Urothelial cancer history disease course



Footnotes

Bladder recurrence after resected UTUC

IVR after UTUC:[1]

- Meta-analysis showed an incidence of 29% (2402 IVR cases from 8275 patients with UTUC)
- Median time to IVR recurrence after UTUC: 22.2 months (range 6.7–56.5 months)

Risk factors for IV:[1]

- Male gender
- Previous bladder
- Preoperative CKD
- Tumor-specific factors: Positive preoperative urinary cytology, ureteral location, multifocality, invasive pT stage, necrosis
- Treatment-specific factors: Laparoscopic RNU, extravesical bladder cuff removal, positive surgical margins

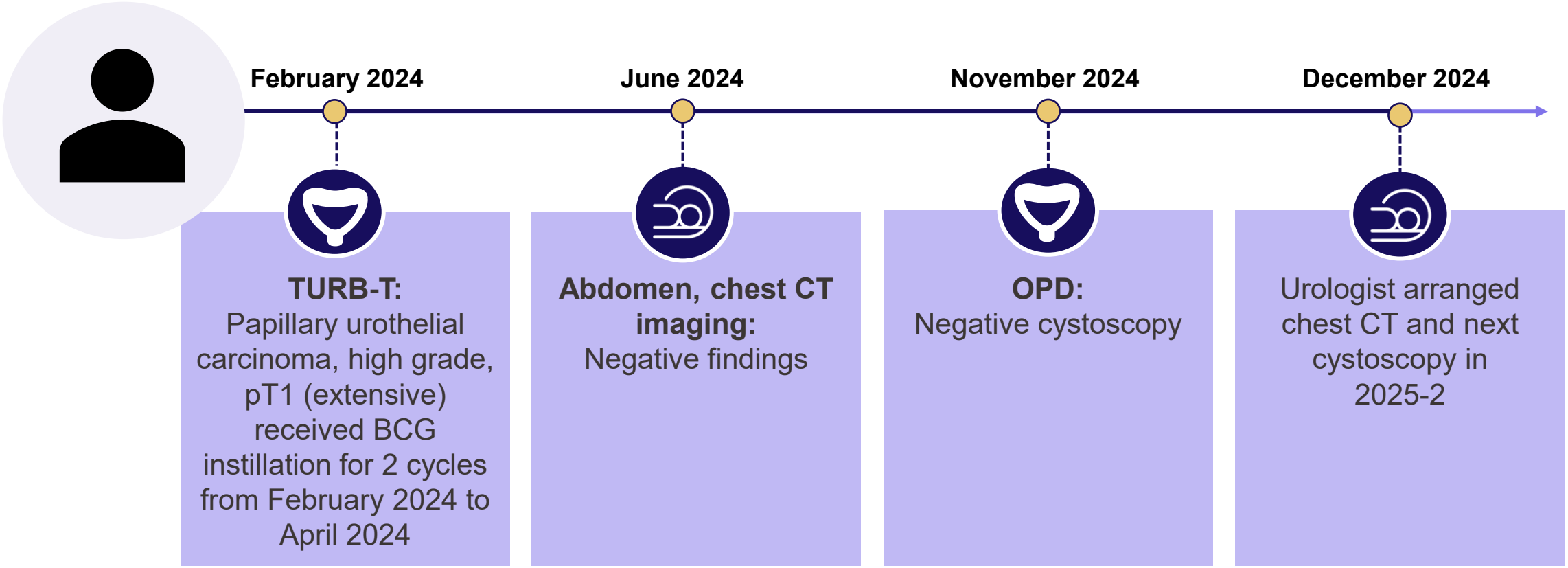
Meta-analysis involving 5 studies involving 2057 patients showed worse outcomes in IVR after UTUC:[2]

- CSS and OS revealed no significant differences between IVR or non-IVR patients
- However, subgroup analysis of pT0-3N0M0 patients suggested that people with IVR had worse CSS (HR = 5.13, $p < 0.0001$) and OS (HR = 4.00, $p < 0.00001$)

CKD, chronic kidney disease; CSS, cancer-specific survival; HR, hazard ratio; IVR, intravesical recurrence; OS, overall survival; pT, pathological tumor; RNU, radical nephroureterectomy; UTUC, upper tract urothelial carcinoma.

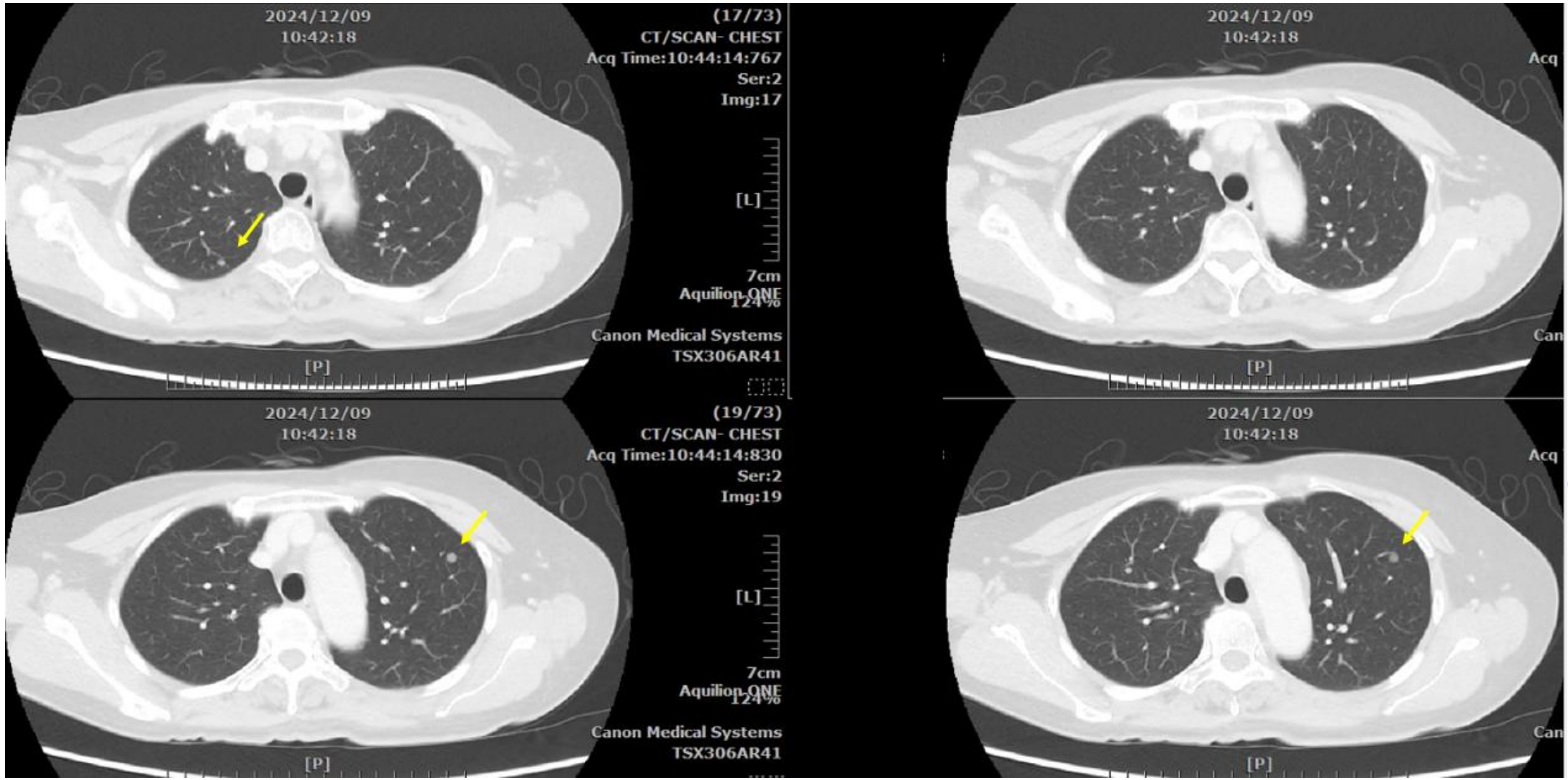
1. Seisen T, et al. Eur Urol 2015;67:1122-1133. 2. Hu H, et al. BMC Urol 2023 21;23:212.

Urothelial cancer history disease course

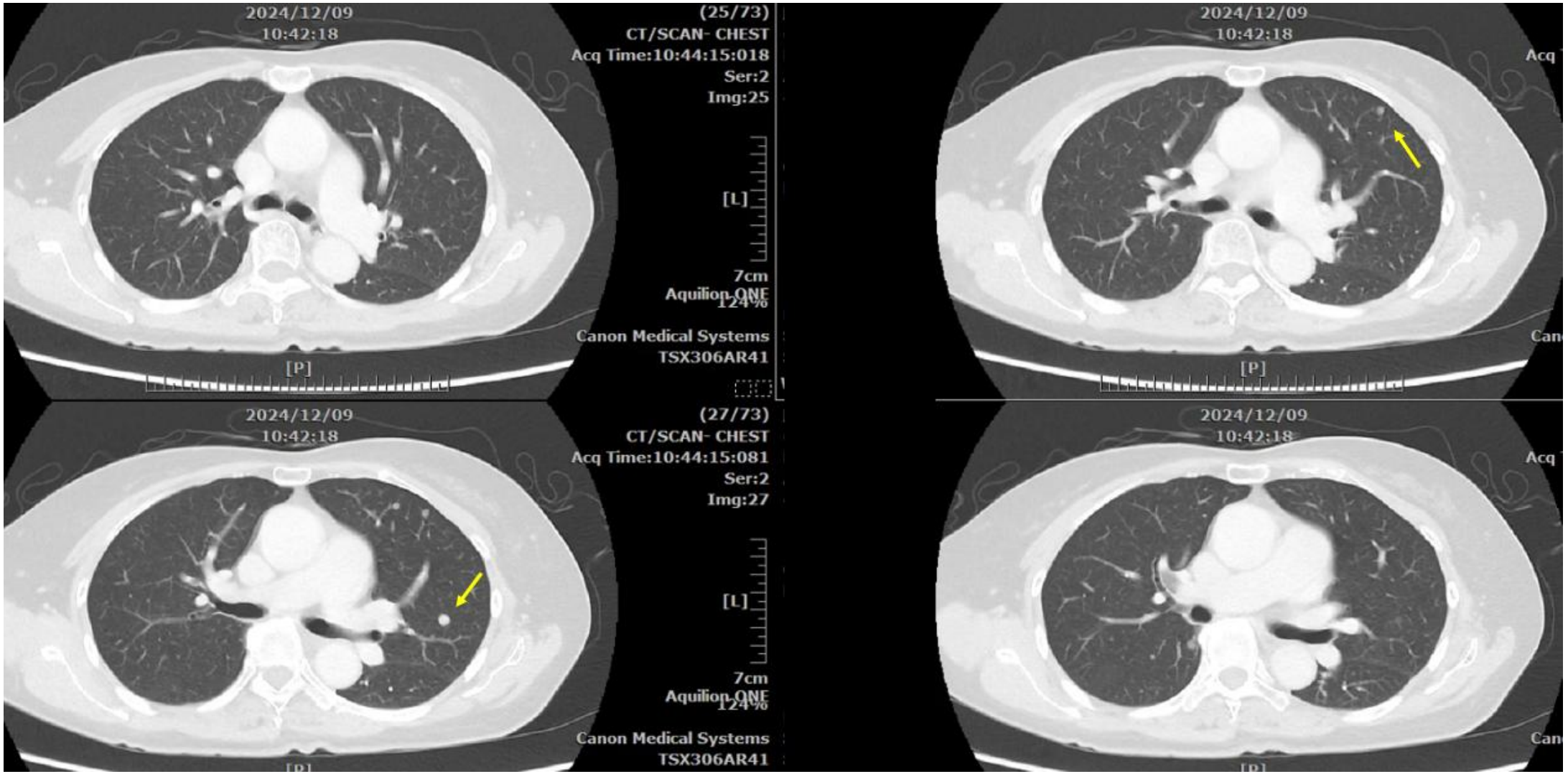


Cystoscopies in May, August, and November 2024 were all negative

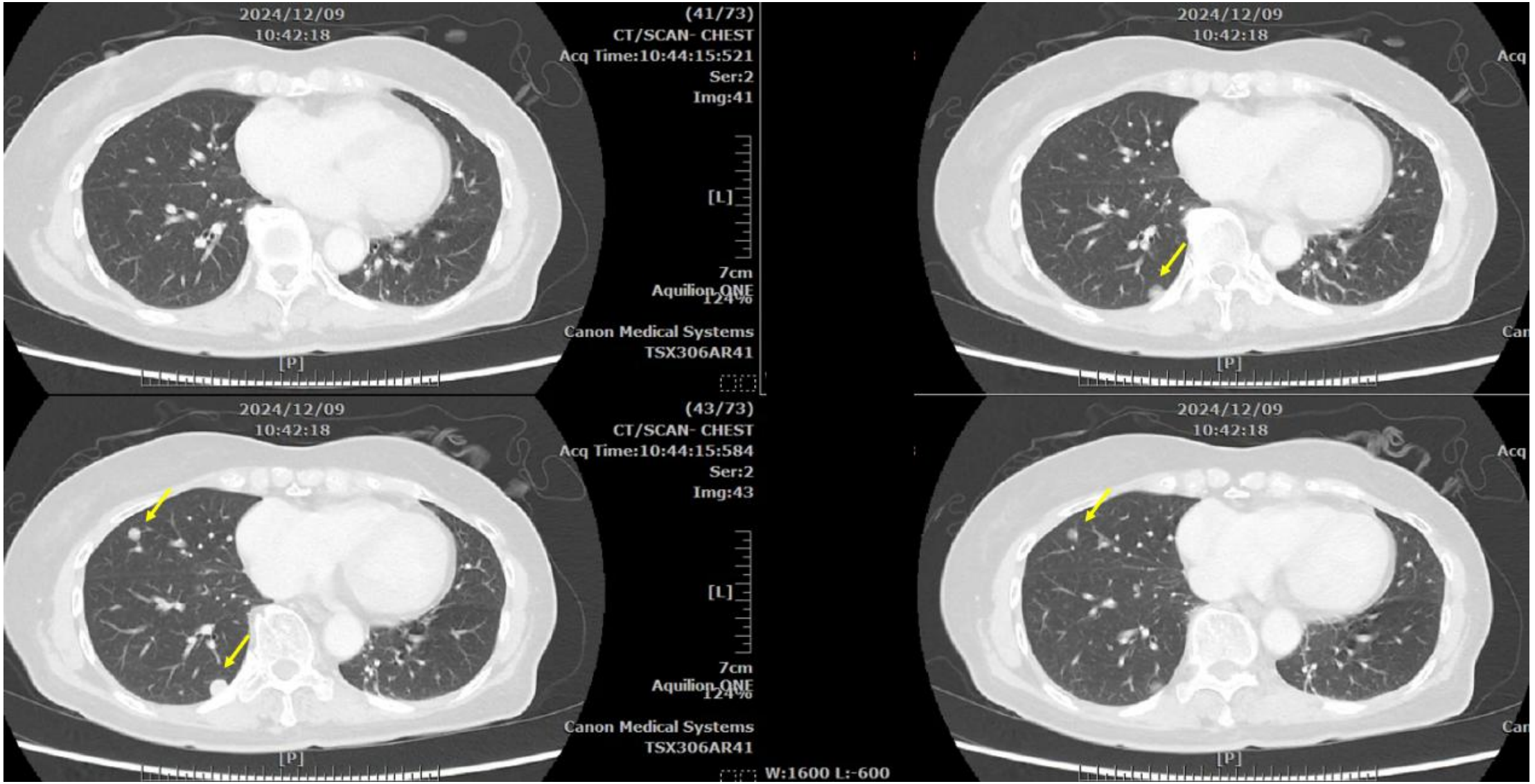
Treatment response



Treatment response



Treatment response



Urothelial cancer history disease course

- Left UTUC s/p left RNU+BCE in 2019
- Bladder recurrence, pT2 in 2023, s/p TURB-T, MMC instillation
- Bladder recurrence, HG T1 in 2024, s/p TURB-T, BCG instillation
- Lung metastases in December 2024
- **Cisplatin eligible, PD-L1 low**

日期	TP	ALB	CA	CACAL	CHOL	BUN	UA	CREA	eGFR(EPI)
24-11-21 11:10	-	-	-	-	-	13	-	-	-
24-11-21 11:10	-	-	-	-	-	-	-	0.74	86.44
24-12-24 13:27	-	-	-	-	-	7	-	0.69	92.15
25-01-05 18:12	-	-	9.7	-	-	8	-	0.75	84.54

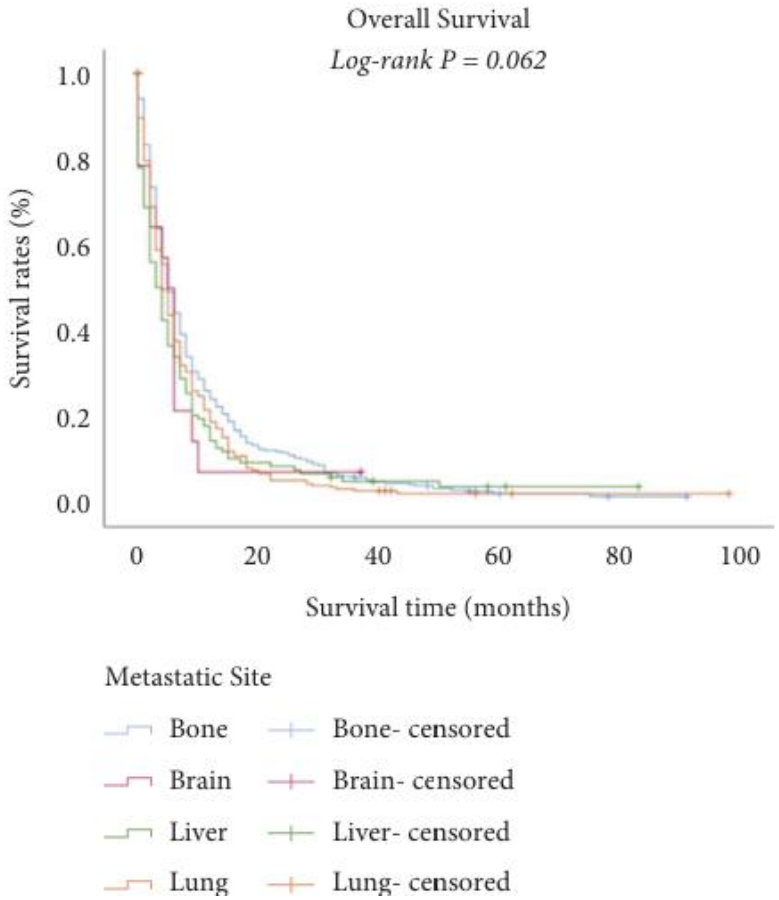
```
PATHOLOGICAL DIAGNOSIS:
PD-L1 expression analysis by immunohistochemistry:
MP No.: PL241178
Block No: S113-08761A
Diagnosis: Papillary urothelial carcinoma, high grade, T1
 (extensive)
Specimen type: Formalin-fixed paraffin-embedded sections
Control slide result: [v]Pass, [ ]Fail
Adequate tumor cells present (>=100 cells): [v]Yes, [ ]No
Antibody used: PD-L1 IHC 22C3 pharmDx (Dako)
Staining platform: Dako Autostainer Link 48
-

Result:
1. Combined Positive Score (CPS): 2
   TC: 2%; IC: 0%  CPS=(2+0)/100 X 100
2. Interpretation:
   [V] CPS < 10 (No PD-L1 expression)
   [ ] CPS >= 10 (High PD-L1 expression)
```

ALB, albumin; BCE, bladder cuff excision; BCG, Bacillus Calmette-Guérin; BUN, blood urea nitrogen; CA, calcium; CACAL, corrected calcium; CHOL, cholesterol; CPS, combined positive score; CREA, creatine; eGFR, IC, immune cells; IHC, immunohistochemistry; MMC, mitomycin C; PD-L1, programmed death-ligand 1; pT, pathological tumor; RNU, radical nephroureterectomy; s/p, status post; TC, tumor cells; TP, total protein; TURB-T, transurethral resection of bladder tumor; UA, uric acid; UTUC, upper tract urothelial carcinoma.

Distant metastases has poor prognosis in bladder cancer

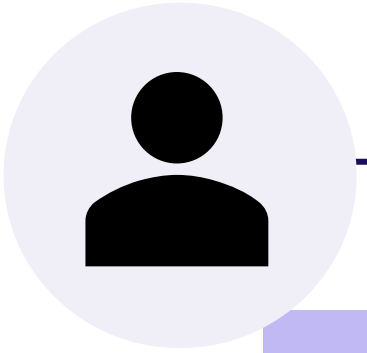
- Analysis from SEER database (3103 stage IV patients), with 1035 metastases cases
- Year of diagnosis: 2010-2015
- The median survival of all patients was 10.0 months, 5 months for patients with bone or brain metastasis, and 4 months for patients with liver or lung metastasis



SEER, Surveillance, Epidemiology and End Results Program.
Liu L et al. *J Oncol* 2022;2:8594022.

Treatment initiation, dosage, and schedule

November 2024 OPD: negative cystoscopy
Urologist arranged chest CT in December 2024 and next cystoscopy in February 2025



January 2025

Presentation

Incidental finding of lung metastases

Further investigations

Whole body bone scan, abdominal CT negative

Chosen therapy

EV+P

Dosing & schedule 50kg

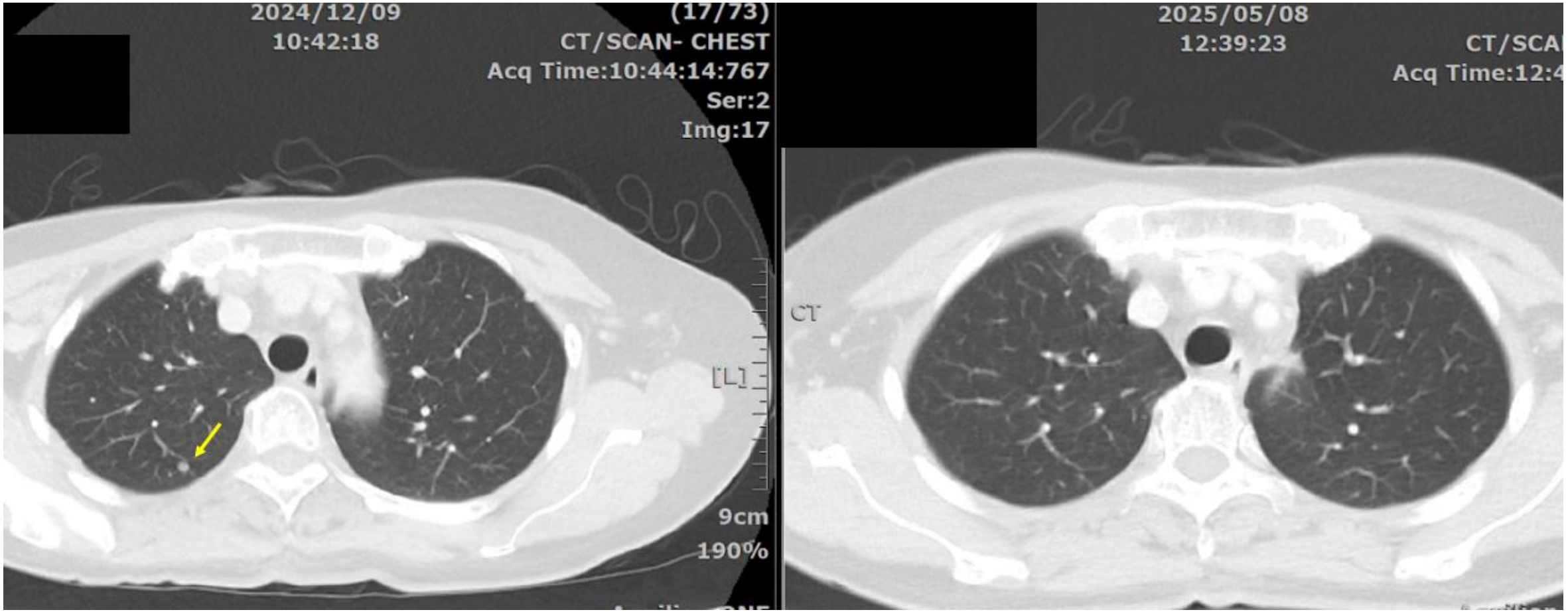
Day 1:
P 200mg + EV (60mg)*

Day 8:
EV 60mg*

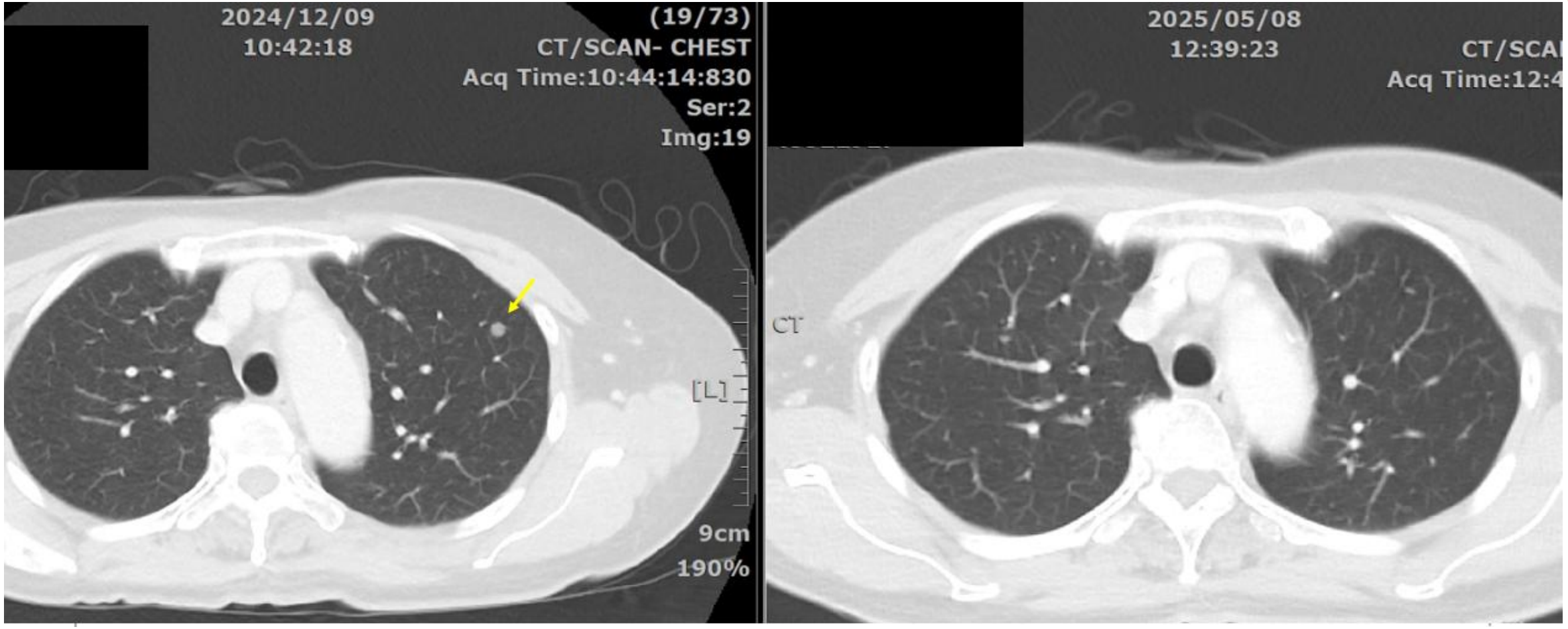
21-day cycles

***Disclaimer: Treatment with EV should always be initiated at the recommended dosage. Always refer to local guidance.**
CT, computed tomography; EV, enfortumab vedotin; P, pembrolizumab.

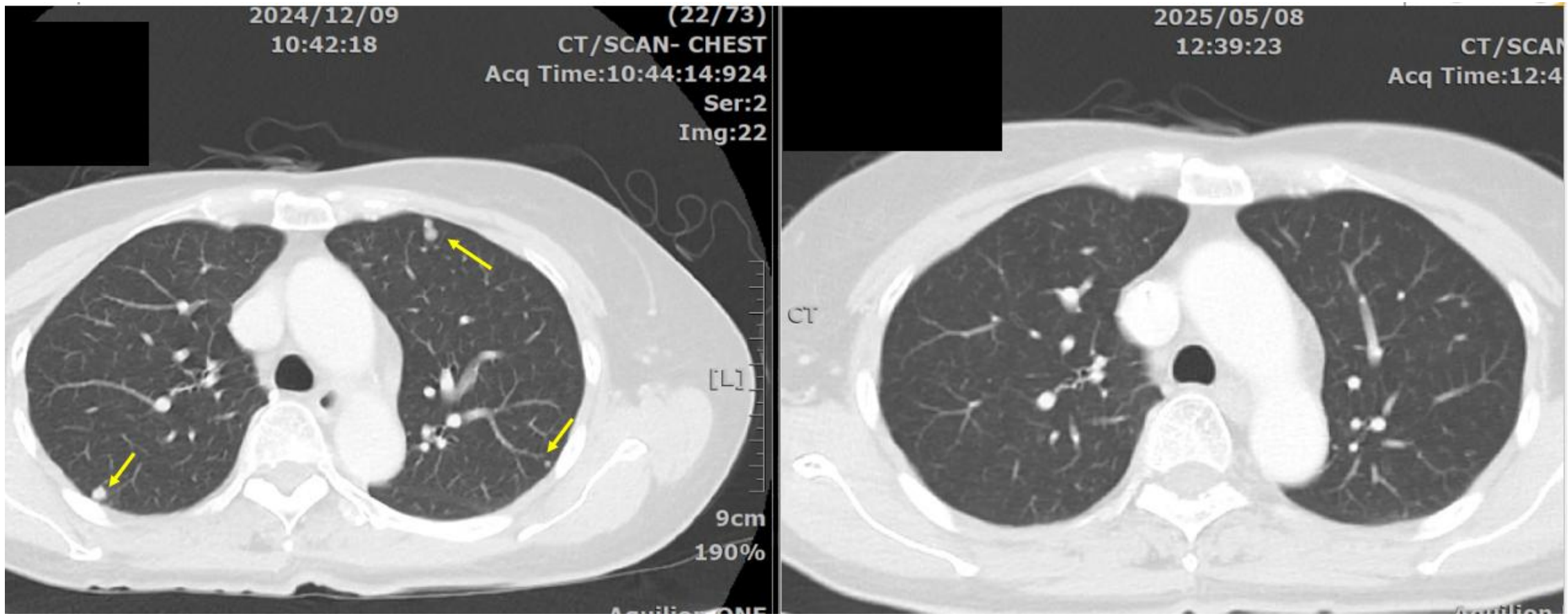
Treatment response



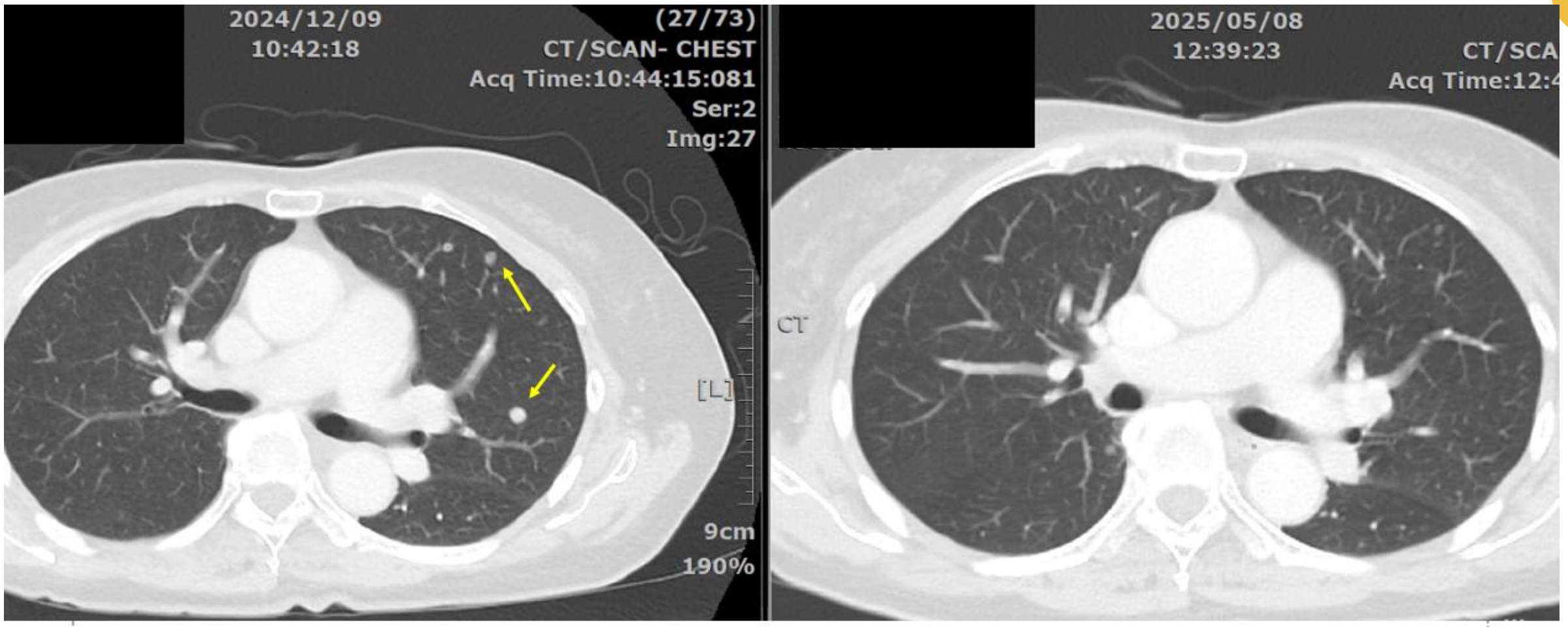
Treatment response



Treatment response



Treatment response



AE presentation and management

S:主觀資料
Stinging eruption on inner thighs for thighs
Asymptomatic erythema on chest when administering chemotherapy

O:客觀資料
Erythematous patches and xerosis on inner thighs
Diffuse erythematous patches on neck
No wounds

AE symptoms:
Skin reaction

AE assessment and grade:
Grade 2

Drug associated with AE:
EV+P

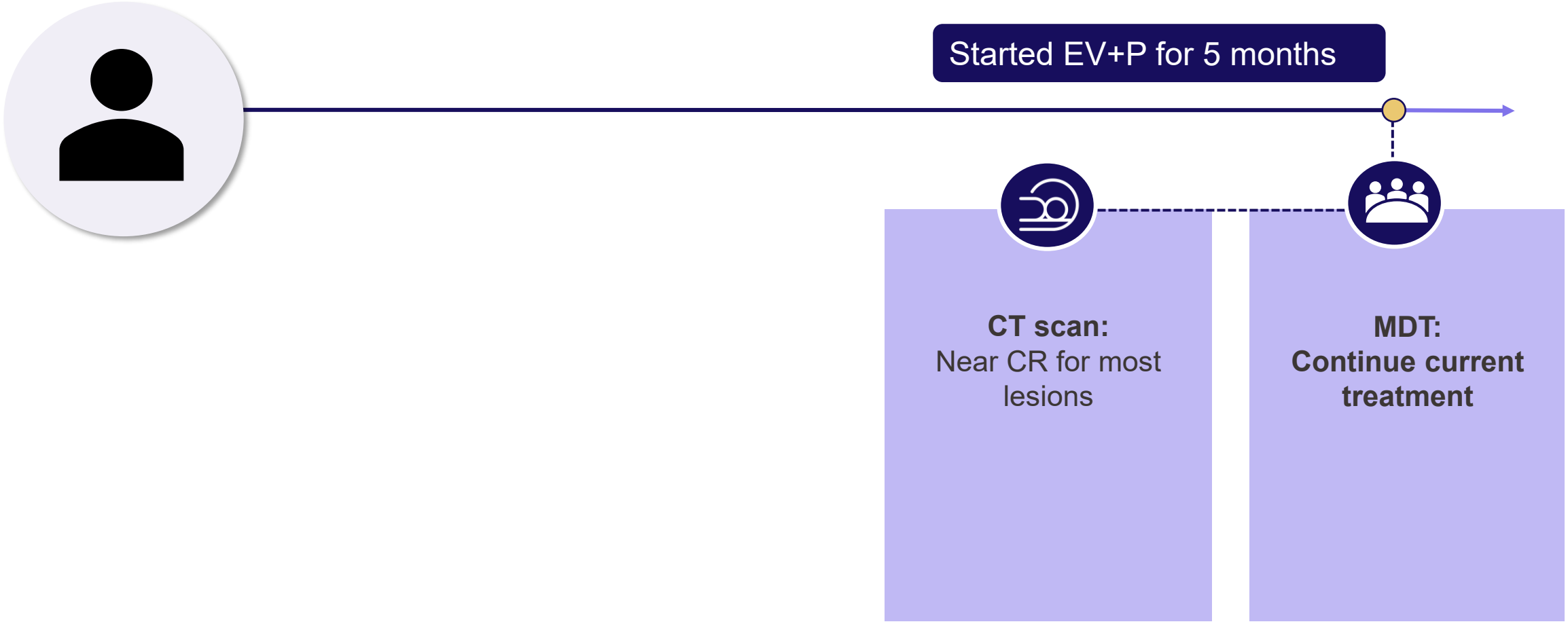
Referral to specialist:
Dermatology

Dose interruption/reduction and duration of this:
None

Management strategies:
Oral antihistamines
topical **ureson**:
(Hydrocortisone 10mg+Urea 100mg/g)

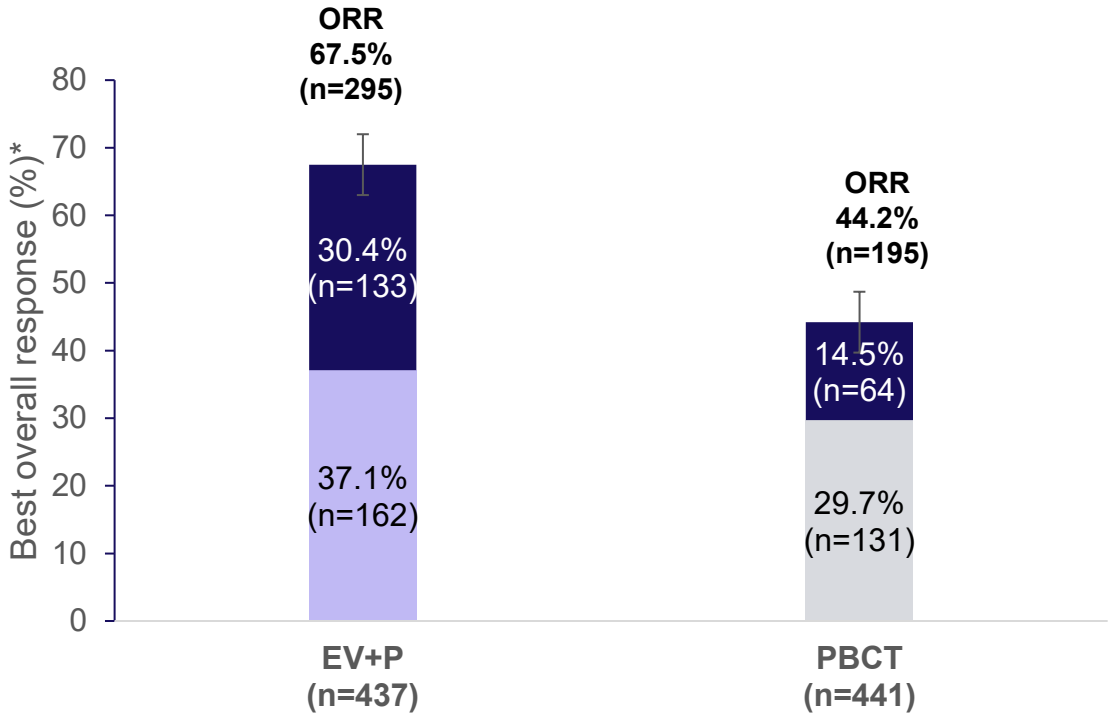
EV, enfortumab vedotin; P, pembrolizumab.

Long-term response to treatment



CR, complete response; CT, computed tomography; EV, enfortumab vedotin; MDT, multidisciplinary team; P, pembrolizumab.

In EV-302, CR rate for patients treated with EV+P was doubled vs. patients treated with PBCT[1,2]



	EV+P (n=437)	PBCT (n=441)	Nominal two-sided P-value
Confirmed ORR (CR or PR), n (%) [95% CI]	295 (67.5) [62.9–71.9]	195 (44.2) [39.5–49.0]	<0.00001†
Best overall response, n (%)			
CR	133 (30.4)	64 (14.5)	
PR	162 (37.1)	131 (29.7)	
SD	83 (19.0)	149 (33.8)	

Footnotes

Summary

EV+P is associated with high response rates in metastatic UC vs. PBCT, including for UTUC[1]

Peripheral neuropathy is an AESI that occurs with use of EV+P. Patients should be monitored and educated on the signs of peripheral neuropathy and managed per the SmPC guidance[2,3]

Skin toxicities may be attributed to both EV and P, topical steroids, urea, antihistamines are usually effective in the majority of cases[2,3]

EV+P is an effective treatment option for a broad patient population, including those with comorbidities and those of special clinical interest, e.g., UTUC, alongside effective management strategies[2,3]

AESI, adverse event of special interest; EV, enfortumab vedotin; P, pembrolizumab; SmPC, Summary of Product Characteristics; UC, urothelial carcinoma; UTUC, upper urinary tract urothelial carcinoma.

1. Bedke J, et al. Presented at ASCO 2025. Abstract 4571; 2. Brower B et al. *Front Oncol* 2024;14:1326715; 3. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics

Genitourinary Masterclass

astellas

Please refer to the Korean PI for PADCEV® (enfortumab vedotin) via the following link or QR Code:

<PADCEV 20mg>

<PADCEV 30mg>

Astellas Pharma Korea., Inc.
(7F Parnas tower, 521, Teheran-ro, Gangnam-gu, Seoul, Republic of Korea)

Footnotes

Genitourinary Masterclass

Best practice sharing: Practical approaches to patient care – Part 1

Professor Daniel Petrylak

Director of Genitourinary Oncology, Yale University Cancer Center, New Haven, USA

EV as first-line therapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer. Combination therapy with pembrolizumab.

EV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 or programmed death-ligand 1 inhibitor, and have received a platinum-containing chemotherapy

EV, enfortumab vedotin.
PADCEV® (enfortumab vedotin). Prescribing Information

Adverse events should be reported.
For Korea, healthcare professionals are asked to report any suspected adverse reactions to Astellas Pharma Korea. Inc
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PADCEV®
enfortumab vedotin
Injection for IV infusion 20 mg & 30 mg vials

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July 2025 | MAT-KR-PAD-2025-00091

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Patient case: Impaired renal function

- Male
- **Age: 63 years**
- **Smoker**
- **Creatine clearance: 40 mL/min**

Initial presentation

Gross hematuria

Further investigations

Cystoscopy: Large bladder mass

TURBT: High grade urothelial cancer with muscle invasion

CT of chest/abdomen/pelvis: Bladder mass and multiple pulmonary nodules

Treatment options

- GemCarbo
- Gem/split dose Cis
- EV+P
- P

Carbo, carboplatin; Cis, cisplatin; CT, computed tomography; EV, enfortumab vedotin; Gem, gemcitabine; P, pembrolizumab; TURBT, transurethral resection of bladder tumour.

Question for the audience

What dose adjustments are required for patients with renal impairment initiating treatment with EV?

- **A** Dose reduction by one level to 1.0 mg/kg
- **B** No dose reductions are needed, initiate at 1.25 mg/kg
- **C** Do not initiate treatment with EV
- **D** Dose reduction by two levels to 0.75 mg/kg

EV, enfortumab vedotin.

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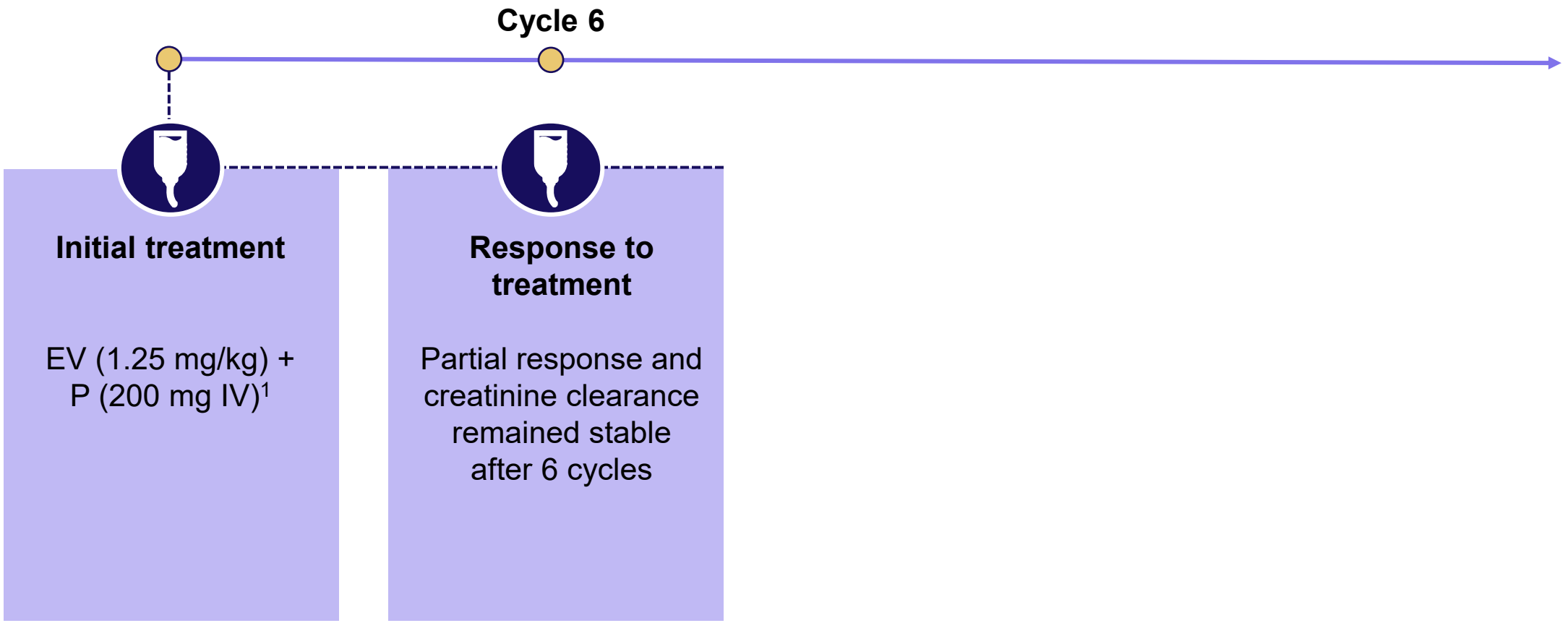
EV, enfortumab vedotin.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

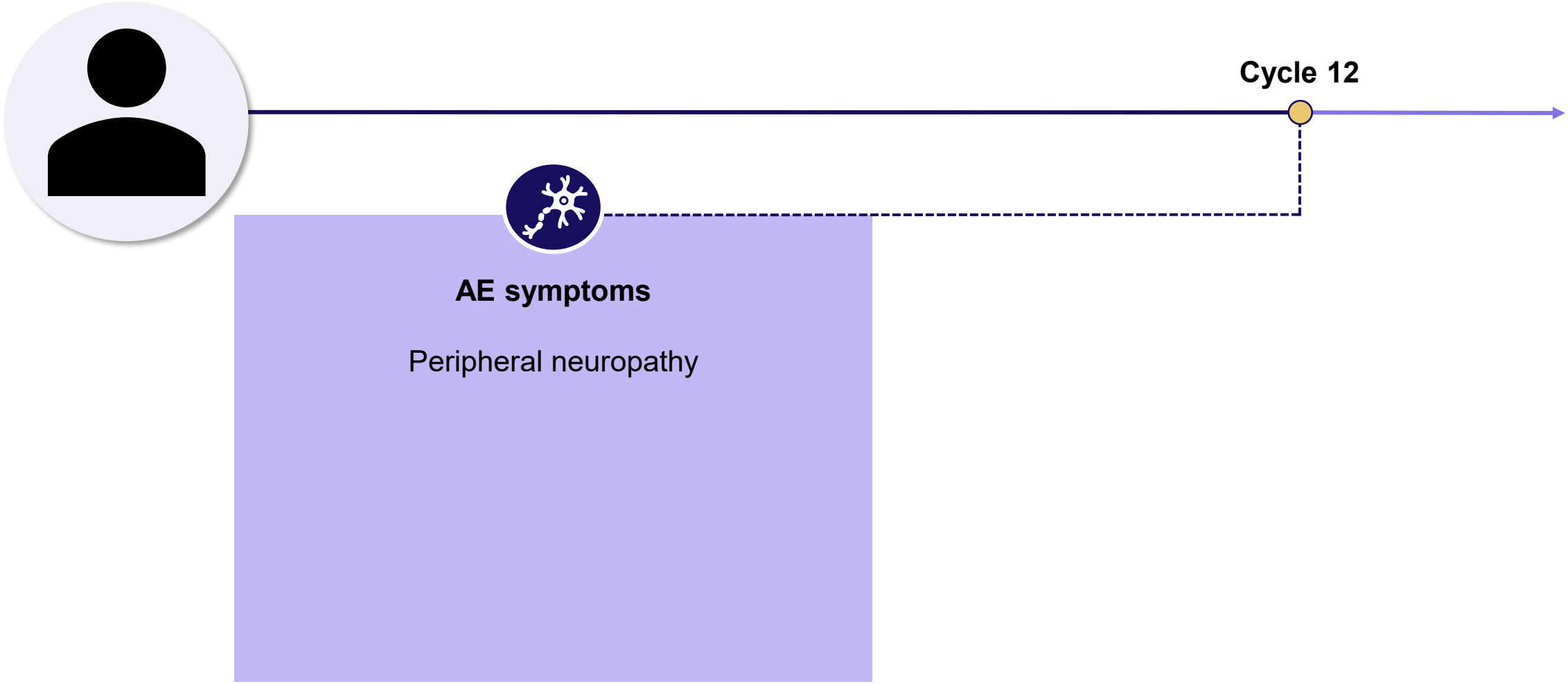
Treatment initiation and response to treatment



EV, enfortumab vedotin; P, pembrolizumab.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

AE presentation and management: Peripheral neuropathy



AE, adverse event.

It is important we understand the safety profile of EV+P to stay ahead of AESIs

Skin toxicities[1,2]

Incidence: 70%
Grade ≥3: 17%

Severe skin reactions:[1]

1.7 months

Range: 0.1–17.2 months

Peripheral neuropathy[1–3]

Incidence: 63.2%
Grade ≥3: 6.8%

Grade ≥2:[3]

6 months

Range: 0.3–25 months

EV-302 trial exclusion criteria:[4]

Ongoing sensory or motor neuropathy Grade ≥2

Hyperglycemia[1–3]

Incidence: 13.0%
Grade ≥3: 8.9%

Any grade:[3]

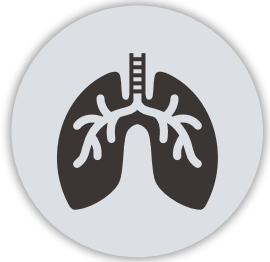
0.5 months

Range: 0.3–3.5 months

EV-302 trial exclusion criteria:[4]

Uncontrolled diabetes, defined as HbA_{1c} ≥8% or HbA_{1c} 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained

Pneumonitis/ILD[1,2]



Incidence: 10.3%
Grade ≥3: 3.5%*

Any grade:[1]

4 months

Range: 0.3–26.2 months

EV-302 trial exclusion criteria:[4]

History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis

Ocular AEs[1–3]

Incidence: 21.4%

EV-302 trial exclusion criteria:[4]

Active keratitis or corneal ulcerations

Median time to onset

Disclaimers: EV+P may not be approved in your region. This content is shared to support proactive AE management of EV (as monotherapy or in combination), not to highlight efficacy. Please refer to local guidelines for appropriate use. PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment). *Two patients experience a fatal event of pneumonitis/ILD.[1]

AE, adverse event; AESI, adverse event of special interest; EV, enfortumab vedotin; HbA_{1c}, glycated hemoglobin; ILD, interstitial lung disease; P, pembrolizumab; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. KEYTRUDA® (pembrolizumab). Summary of Product Characteristics; 3. Brower B et al. *Front Oncol* 2024;14:1326715;
4. Powles T et al. *N Engl J Med* 2024;390:875–888 (protocol).

PN: Risk factors and monitoring

Median time to onset of Grade ≥2 PN:[1]

6 months

PN is an AESI associated with EV, though it may also occur with P.[1,2] In the EV-302 trial, **63.2% of patients developed EV-related PN, of which 6.8% developed Grade ≥3 PN**[2,3]

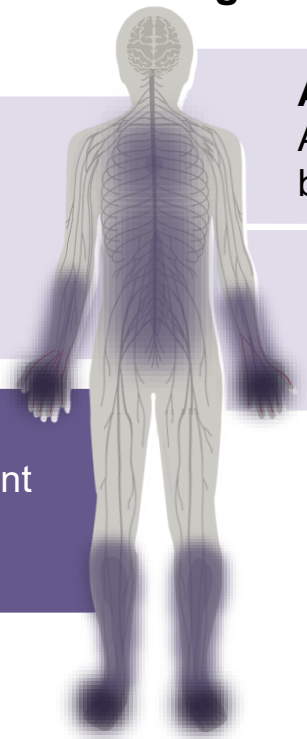
General risk factors[4,5]*

- Pre-existing neuropathy
- Uncontrolled diabetes mellitus
- Pre-existing infection (e.g., HIV)
- Age (≥75 years)
- Family history of neuropathy
- Spinal involvement of mUC
- Non-malignant spinal disease
- Liver/thyroid/kidney disorders
- Autoimmune disease
- Vitamin deficiency
- Smoking
- Increased BMI
- Alcohol abuse

Screening questions for PN are recommended at each visit for patients receiving EV+P treatment,[1] as PN results from damage caused by anti-cancer therapies[5]

Sensory effects[4]
Typically affect hands and feet

Autonomic effects[4]
Affect involuntary bodily processes



Motor effects[4]
Can progress from sensory effects

Conduct functional assessment of fine motor skills: Observe patient buttoning, zipping, or threading a needle[5]

Conduct functional assessment of gait and balance and assess lower-extremity strength and sensation[5]

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*In addition to exposure to neurotoxic agents, such as anti-cancer therapies.[1]

AESI, adverse event of special interest; BMI, body mass index; EV, enfortumab vedotin; HIV, human immunodeficiency virus; mUC, metastatic urothelial carcinoma; P, pembrolizumab; PN, peripheral neuropathy.

1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. Powles T et al. *N Engl J Med* 2024;390:875–888 (supplementary appendix); 3. Powles T et al. *N Engl J Med* 2024;390:875–888;
4. Jordan B et al. *Ann Oncol* 2020;31:1306–1319; 5. Pace A et al. *Clin J Oncol Nurs* 2021;25.

SmPC management guidance

AESI	Severity	Dose modification
Peripheral neuropathy	**Grade ≥3**	Permanently discontinue
	Grade 2	• Withhold until Grade ≤1 • For first occurrence, resume treatment at the same dose level • For a recurrence, withhold until Grade ≤1, then resume treatment reduced by one dose level

Dose reduction schedule

Starting dose
1.25 mg/kg*
up to 125 mg

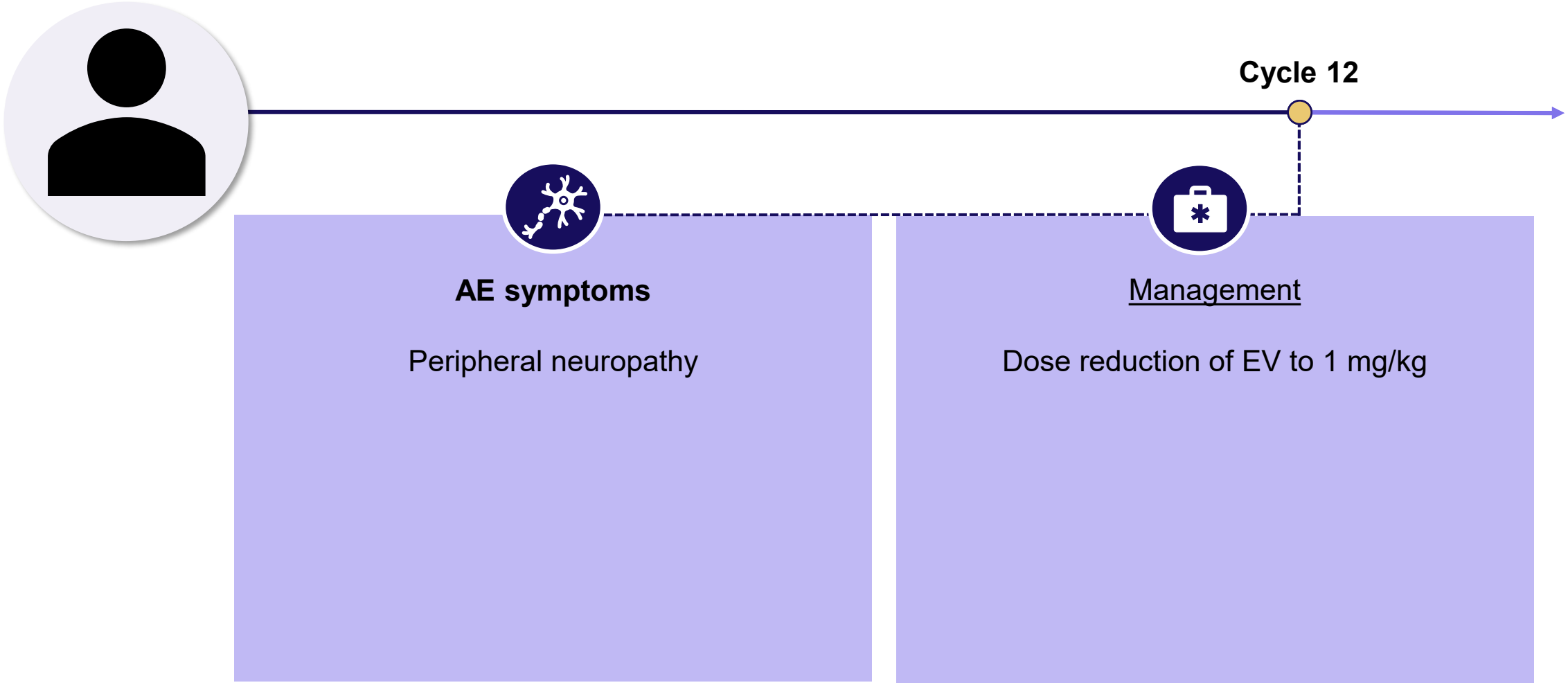
First dose reduction
1.00 mg/kg
up to 100 mg

Second dose reduction
0.75 mg/kg
up to 75 mg

Third dose reduction
0.50 mg/kg
up to 50 mg

*Up to a maximum of 125 mg for patients weighing ≥100 kg.
AESI, adverse event of special interest; SmPC, Summary of Product Characteristics.
PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

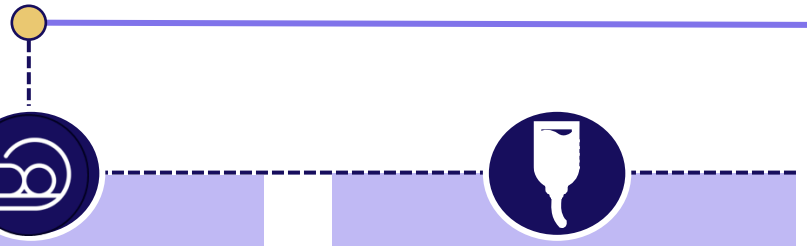
AE presentation and management: Peripheral neuropathy



AE, adverse event; EV, enfortumab vedotin.

Further investigations

5 months after initiating treatment



Further investigations

CT of chest/abdomen/pelvis:
New liver metastases

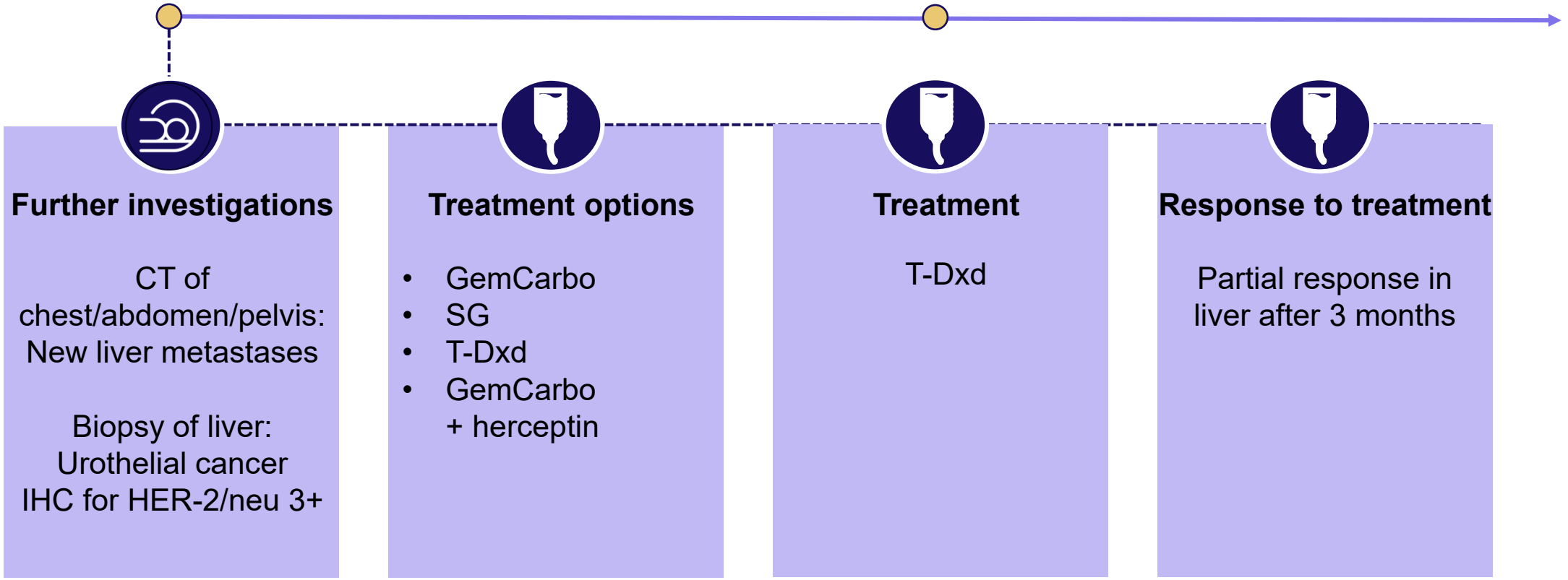
Biopsy of liver:
Urothelial cancer
IHC for HER-2/neu 3+

Treatment options

- GemCarbo
- SG
- T-Dxd
- GemCarbo + herceptin

Carbo, carboplatin; CT, computed tomography; EV, enfortumab vedotin; Gem, gemcitabine; IHC, immunohistochemistry; P, pembrolizumab; SG, sacituzumab govitecan; T-Dxd, trastuzumab deruxtecan.

Treatment initiation and response



Carbo, carboplatin; CT, computed tomography; EV, enfortumab vedotin; Gem, gemcitabine; IHC, immunohistochemistry; P, pembrolizumab; SG, sacituzumab govitecan; T-Dxd, trastuzumab deruxtecan.

Question for the audience

Is the primary route of elimination of EV renal?

- **A** Yes, it is excreted renally
- **B** No, it is metabolized by the liver
- **C** Unsure

EV, enfortumab vedotin.

Question for the audience

Is the primary route of elimination of EV renal?

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- **B** No, it is metabolized by the liver[1]
- **C** Unsure

EV, enfortumab vedotin.

1. Maiorano BA, et al. *Front Oncol.* 2023:13:1254906.

Summary

There are no contraindications or dose adjustments required for EV in patients with impaired renal function. This includes mild, moderate, or severe renal impairment[1]*

PN is a frequent, dose-limiting toxicity associated with EV use; however, early recognition of treatment-emergent PN and prompt intervention with the use of dose modifications provides the best chance for resolution, without impacting the ability to maintain response to EV[1]

EV+P is an effective treatment option for a broad patient population. Early identification and effective care can help ensure patients are able to continue to receive their treatment, to ensure patients receive optimal treatment outcomes[1,2]

*Mild (CrCL >60–90 mL/min), moderate (CrCL 30–60 mL/min), and severe (CrCL <15 mL/min).[1]
CrCL, creatinine clearance; EV, enfortumab vedotin; P, pembrolizumab; PN, peripheral neuropath.
1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. Brower B et al. *Front Oncol* 2024;14:1326715

Genitourinary Masterclass

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PI, Prescribing Information.

Genitourinary Masterclass

Best practice sharing: Practical approaches to patient care – Part 2

Prof. Jungmin Jo

South Korea

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July 2025 | Job code:MAT-KR-PAD-2025-00093

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Introducing JHH

JHH

- Asian, male
- **Age: 83** years
- **ECOG PS: 1**
- **GFR: 59** mL/min
- **BMI: 20** kg/m^2
- **HbA1c: 6.1** mmol/mol (%)

Lifestyle: Low physical activity due to comorbidities

Employment status/job:

Not currently employed

Family history of cancer: None

Comorbidities: HF R/O CAOD

Concomitant medications:
Spironolactone, bisoprolol, empagliflozin

Any other relevant medical history:
Folic acid

Habits:

Low physical activity due to age-related limitations; slow walking because of past right leg fracture

Priorities:

Keen to receive life-extending treatment

BMI, body mass index; CAOD, coronary artery occlusive disease; ECOG, Eastern Cooperative Oncology Group; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; HF, heart failure, PS, performance status; R/O, result of.

Treatment initiation, dosage, and schedule

[July 2024]

Initial presentation
Hematuria

Further investigations
CT: Bladder cancer with right distal ureter and right pelvic wall inv
Multiple metastases in LNs, both lungs, right pleural

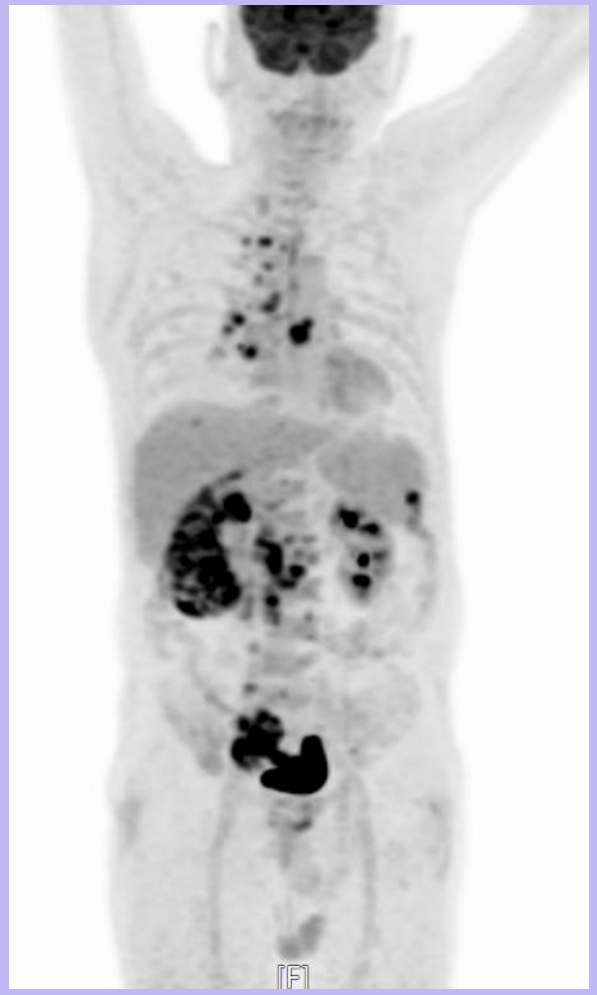
Chosen therapy
s/p oTURB (2024/7/22) pT1c HG
s/p oBCG
s/p right PCN (2025/3/10)

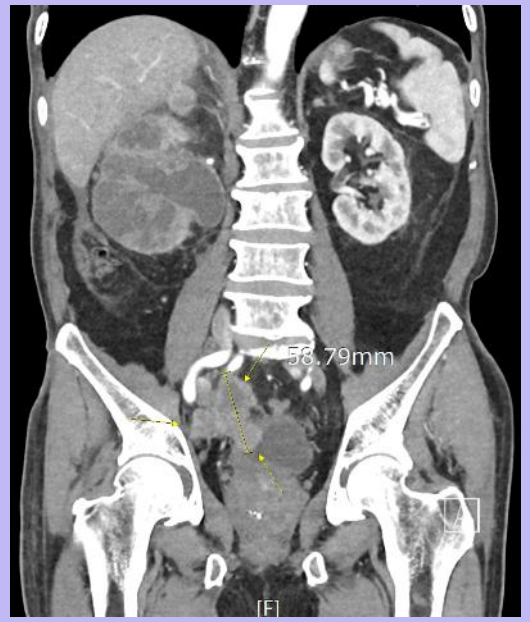
Enfortumab vedotin + pembrolizumab as 1L treatment

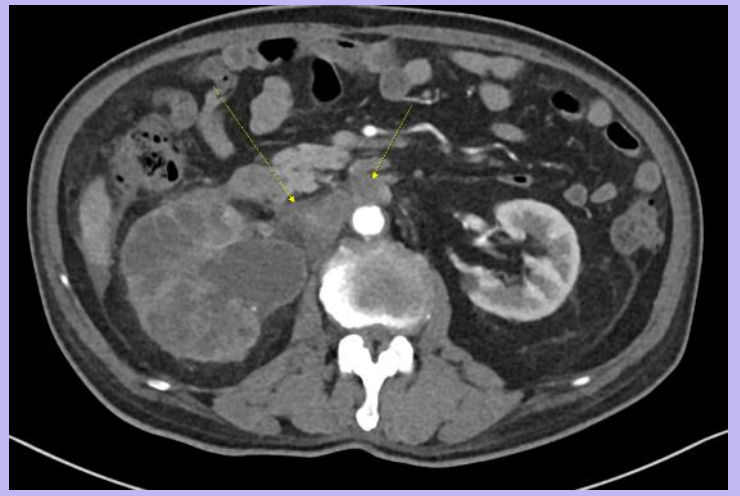
Dosing and schedule
EV 1 mg/kg on Day 1, 8 (d/t age and cost)
Pembrolizumab 200 mg Day 1 Q3W

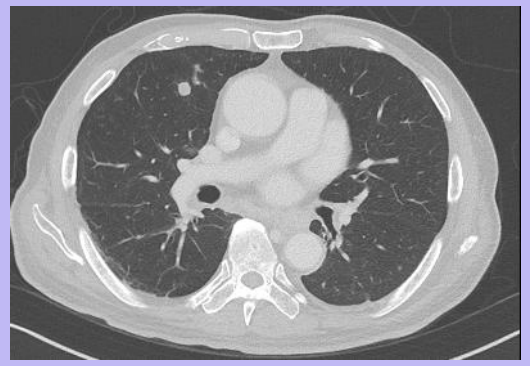
Treatment with EV should always be initiated at the recommended dosage. Always refer to local guidance.
1L, first line; BCG, Bacillus Calmette–Guerin; CT, computed tomography; EV, enfortumab vedotin; HG, histological grade; inv, invasion; LN, lymph node; PCN, percutaneous nephrostomy; Q3W, every 3 weeks; s/p, status post; TURB, transurethral resection of bladder.

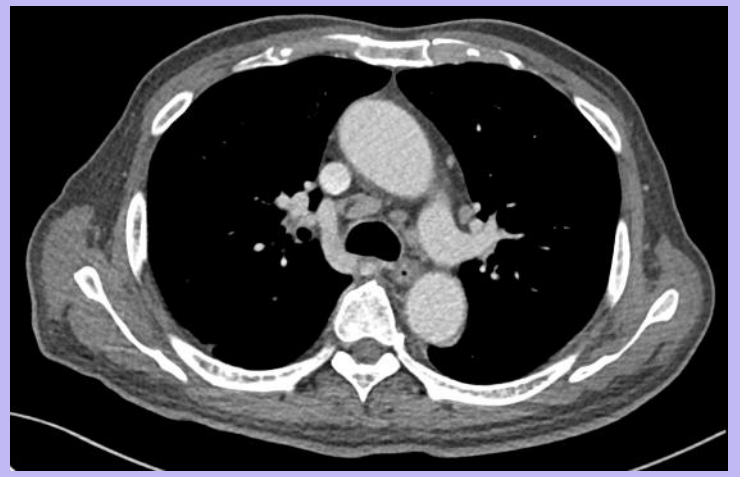
Initial patient response to treatment [1/2]





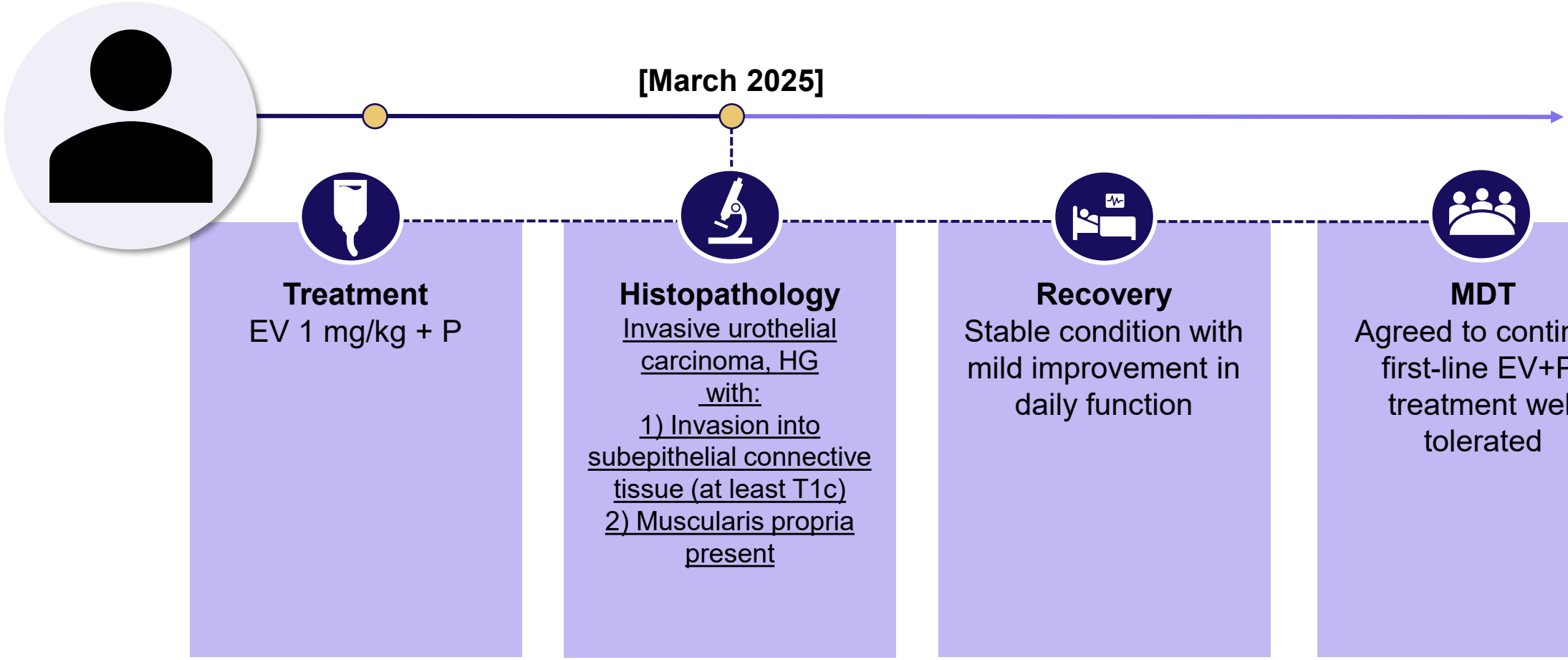






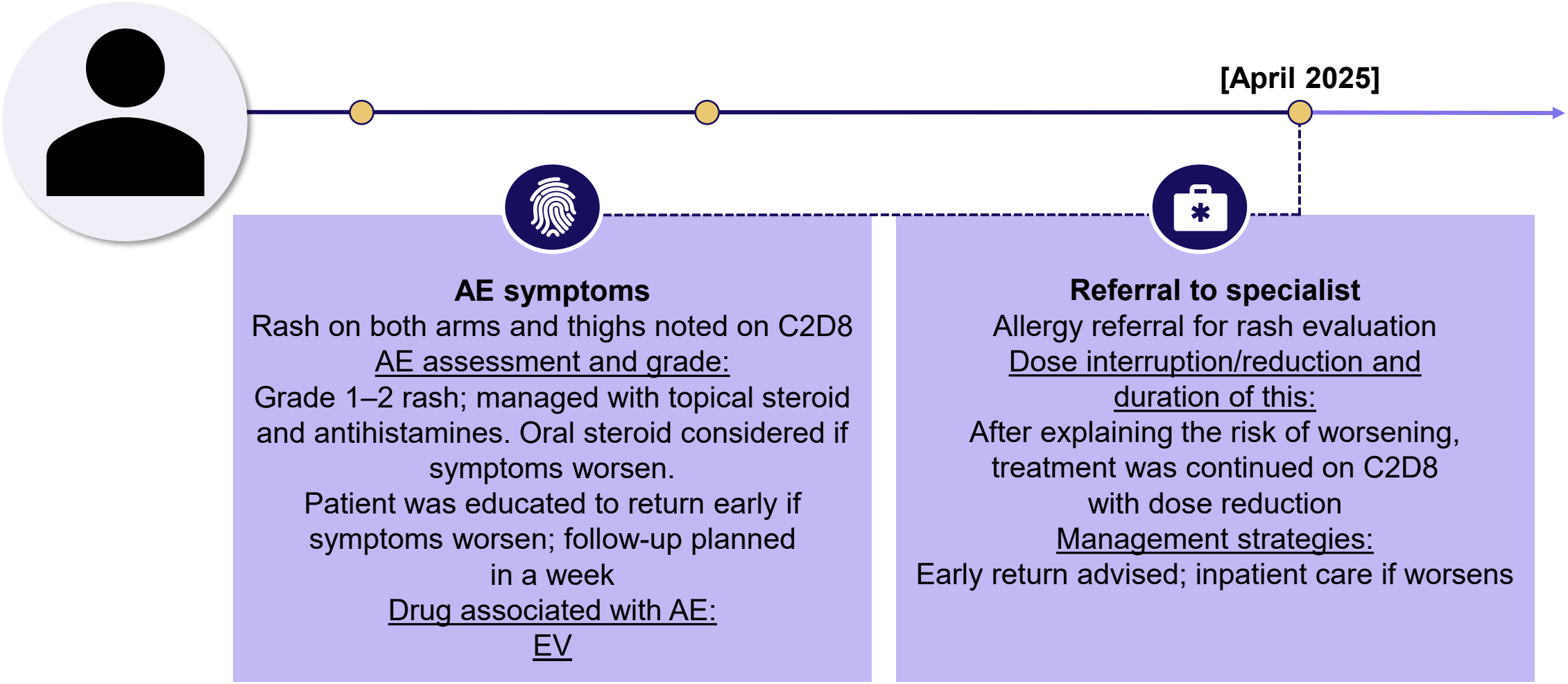
Images courtesy of Prof. Jungmin Jo with permission of the patient.

Initial patient response to treatment [2/2]



EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; HG, histological grade; MDT, multidisciplinary team; P, pembrolizumab.

AE presentation and management: Skin toxicity

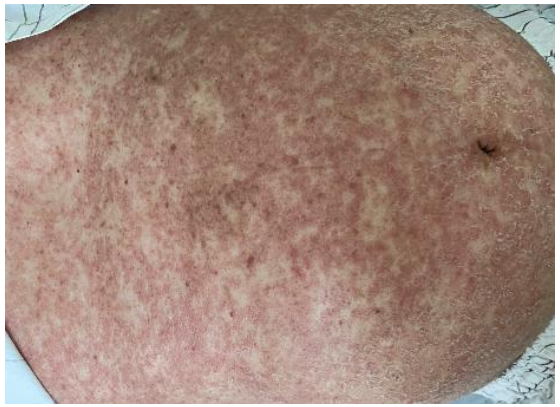


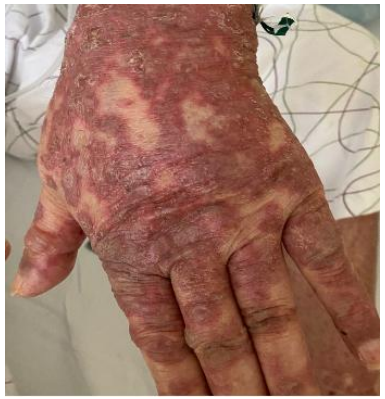
AE, adverse event; C2D8, Cycle 2 Day 8; EV, enfortumab vedotin.

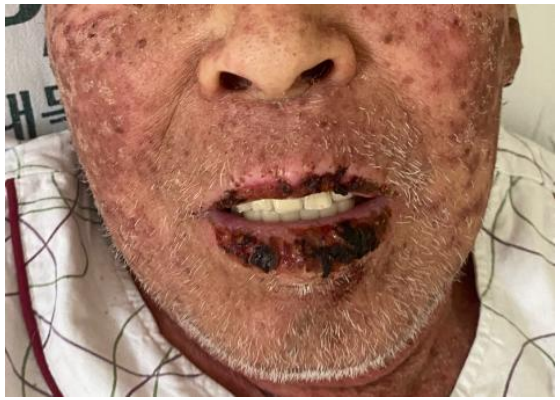
AE management: Skin toxicity

[May 2025]

After a week, skin reaction worsened to Grade 3; SJS could not be ruled out





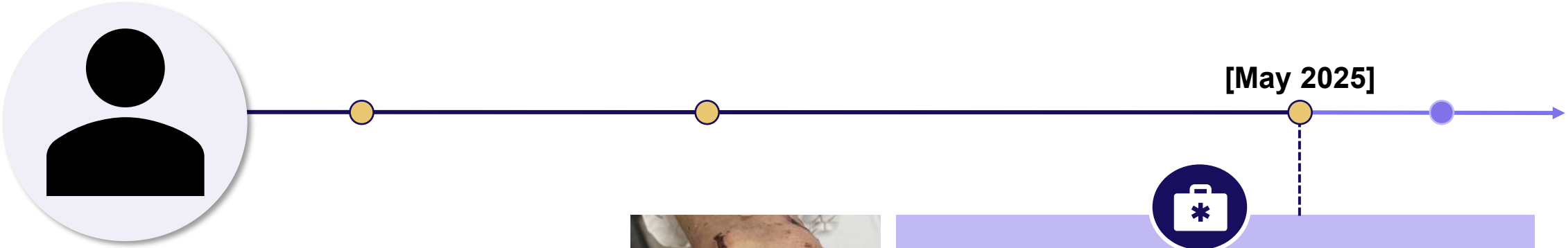


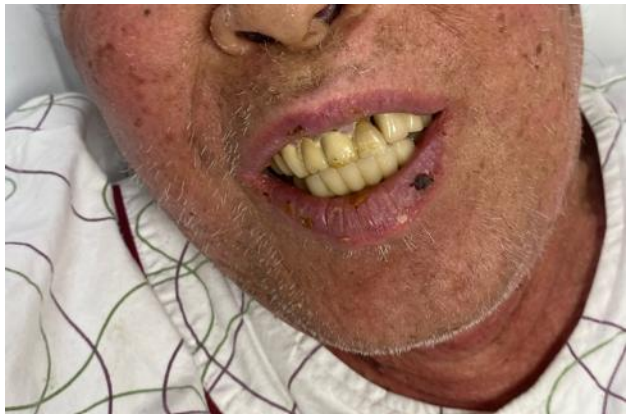
Effect of AE management strategies on AE:
Admission
High-dose steroid initiated, followed by tapering
Allergy: Monitor closely for progression of erythema multiforme to SJS

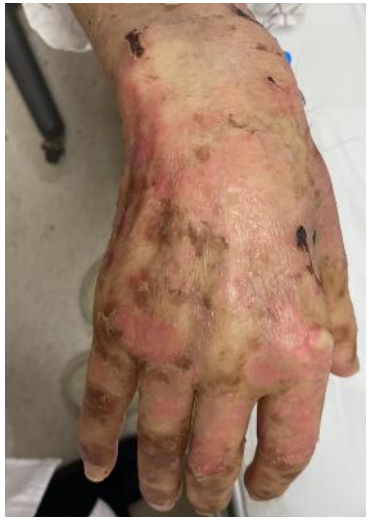
Subsequent treatment:
Permanent discontinuation was recommended by the allergy team

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).
Images courtesy of Prof. Jungmin Jo with permission of the patient.
AE, adverse event. SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

AE management: Skin toxicity







After 2 weeks of hospitalization, the patient was discharged on oral steroids following dose tapering

<u>Effect of AE management strategies on AE:</u>
High-dose steroid initiated, followed by tapering
Allergy: Monitor closely for progression of erythema multiforme to SJS

<u>Subsequent treatment:</u>
Consider switching to gemcitabine + cisplatin after recovery

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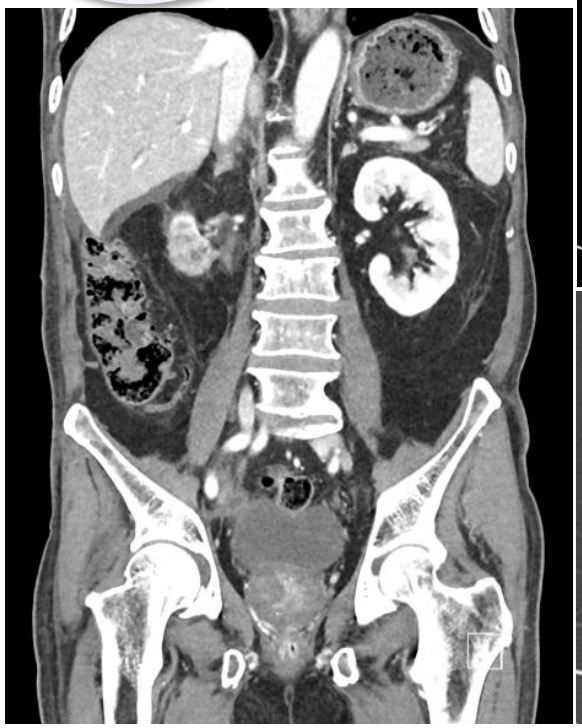
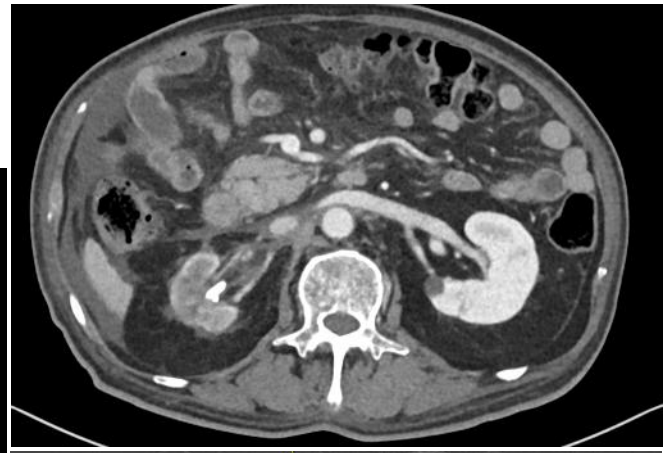
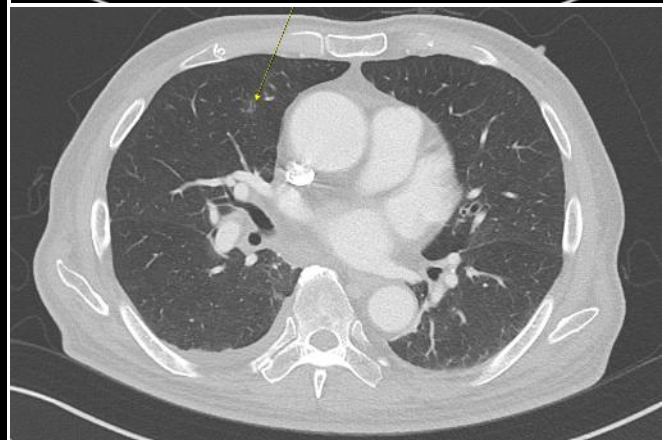
Images courtesy of Prof. Jungmin Jo with permission of the patient.
AE, adverse event; SJS, Stevens–Johnson syndrome; SJS, Stevens–Johnson syndrome.

Long-term response to treatment







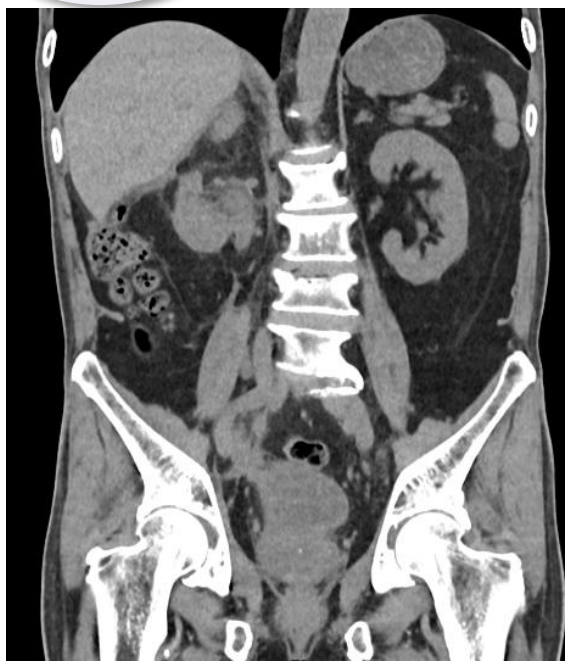
[May 2025]

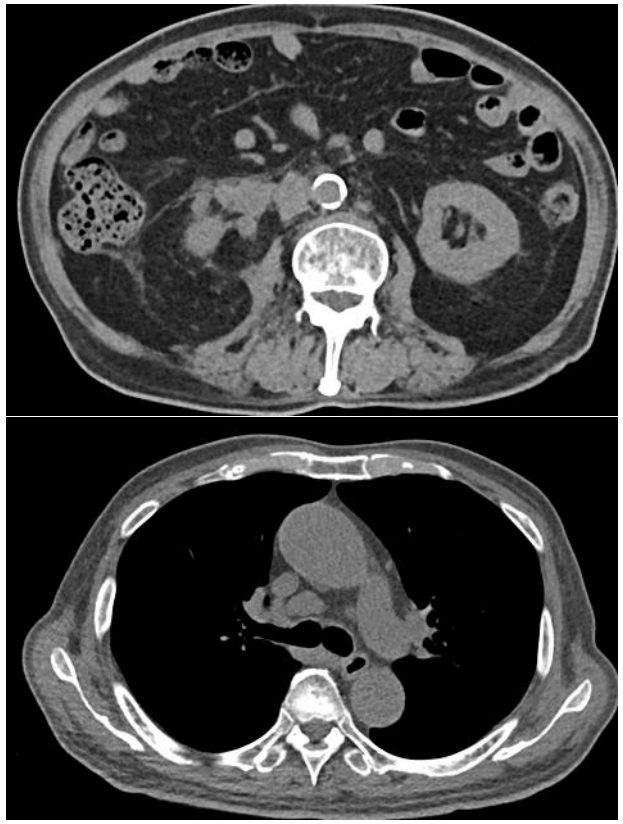
CT scan
Near complete resolution of previous multiple probably metastatic nodules in both lungs
Marked decrease of overall tumor burden

MDT
Switching to CisGem after recovery

Images courtesy of Prof. Jungmin Jo with permission of the patient.
Cis, cisplatin; CT, computed tomography; Gem, gemcitabine; MDT, multidisciplinary team.

Long-term response to treatment





[June 2025]

CT scan
Disease progression occurred 2 months after discontinuation of EV+P

MDT
CisGem started on June 16; rechallenge to be considered based on response

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Images courtesy of Prof. Jungmin Jo with permission of the patient.
Cis, cisplatin; CT, computed tomography; EV+P, enfortumab vedotin plus pembrolizumab; Gem, gemcitabine; MDT, multidisciplinary team.

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Incidence: 70%
Grade ≥3: 17%

Peripheral neuropathy[1–3]

Incidence: 63.2%
Grade ≥3: 6.8%

Hyperglycaemia[1–3]

Incidence: 13.0%
Grade ≥3: 8.9%

Pneumonitis/ILD[1,2]

Incidence: 10.3%
Grade ≥3: 3.5%*

Ocular AEs[1–3]

Incidence: 21.4%

Median time to onset

Severe skin reactions:[1]

1.7 months

Range: 0.1–17.2 months

Grade ≥2:[3]

6 months

Range: 0.3–25 months

EV-302 trial exclusion criteria:[4]

Ongoing sensory or motor neuropathy Grade ≥2

Any grade:[3]

0.5 months

Range: 0.3–3.5 months

EV-302 trial exclusion criteria:[4]

Uncontrolled diabetes, defined as HbA1c ≥8% or HbA1c 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained

Any grade:[1]

4 months

Range: 0.3–26.2 months

EV-302 trial exclusion criteria:[4]

History of idiopathic pulmonary fibrosis, organising pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis

EV-302 trial exclusion criteria:[4]

Active keratitis or corneal ulcerations

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).

*Two patients experience a fatal event of pneumonitis/ILD.[1]

AE, adverse event; AESI, adverse event of special interest; EV, enfortumab vedotin; HbA1c, glycated haemoglobin; ILD, interstitial lung disease; P, pembrolizumab.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. KEYTRUDA® (pembrolizumab). Summary of Product Characteristics; 3. Brower B et al. *Front Oncol* 2024;14:1326715;
4. Powles T et al. *N Engl J Med* 2024;390:875–888 (protocol).

Skin toxicities: Risk factors and monitoring

Median time to onset of severe skin reactions:[3]

1.7 months

Most skin-related AEs are mild, transient, and occur early; however, they should still be reported and managed quickly to reduce the risk of progression to a more severe reaction, which may lead to EV+P treatment delays or discontinuation or even be fatal[1–3]

General risk factors for skin reactions to anti-cancer therapy[1,4]

Prior history of:

- Cutaneous reactions to previous anti-cancer therapies
- A dermatological condition
- Allergies
- Dry skin
- Immunosuppression
- Immune-mediated skin conditions
- A high level of sun exposure or radiation treatment
- Advanced age
- Renal and/or hepatic impairment

Patients receiving EV+P should be monitored for skin reactions at each clinic visit, including before each administration[1]

Complete visual inspection and palpation of the skin across the entire body[1,5]

Record and photograph the colour, texture, morphology, distribution, and extent of lesions[5]

Monitor the skin for secondary skin infections[1]

Assess for presence of red flag symptoms (e.g., rash or itching that continues to get worse or comes back after treatment, skin blistering or peeling, mucosal involvement: Painful sores or ulcer in mouth or nose, throat or genital area, fever or flu-like symptoms, and swollen lymph nodes[3]

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).

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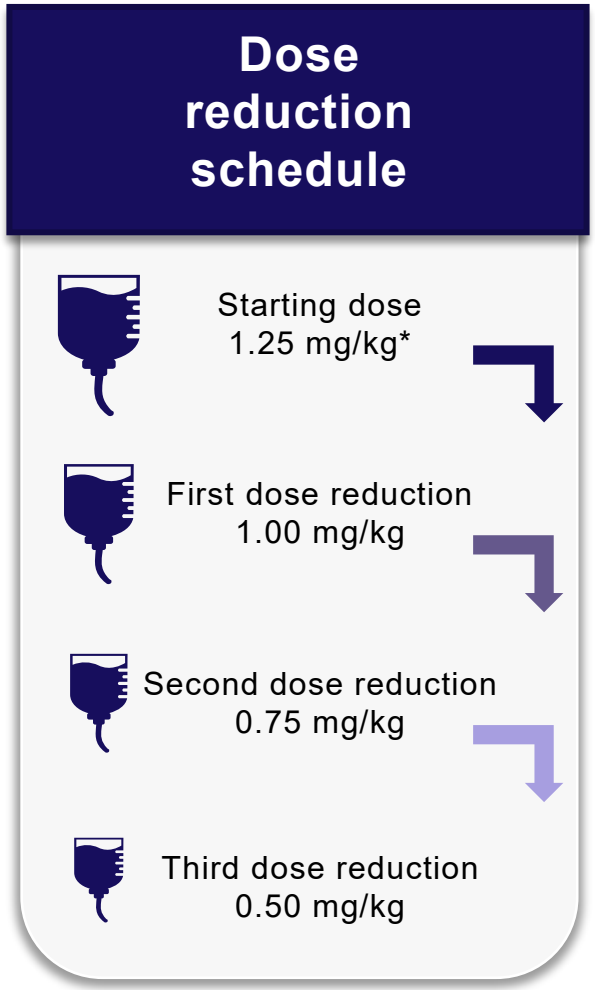
1. Pace A et al. *Clin J Oncol Nurs* 2021;25:E1–E9; 2. Dobry AS et al. *JAAD Case Rep* 2021;14:7–9; 3. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 4. Lacouture ME et al. *Oncologist* 2022;27:e223–e232; 5. Barton-Burke M et al. *Nurs Clin North Am* 2017;52:83–113.

There is established guidance for the management of skin toxicity with EV+P

AESI	SmPC management guidance
Skin reactions	Topical **corticosteroids and antihistamines** can be considered for **mild to moderate skin reactions**
	For **suspected SJS or TEN**, or in case of **bullous lesion** onset, **withhold treatment immediately and refer to specialist care**
	For **Grade 2 worsening, Grade 2 with fever, or Grade 3 skin reactions**, treatment should be **withheld until Grade ≤1** and **referral for specialist care** should be considered. Treatment should be **resumed at the same dose level or consider dose reduction** by one dose level
	Permanently discontinue EV for **confirmed SJS** or **TEN**, or **Grade 4** or **recurrent Grade 3** skin reactions



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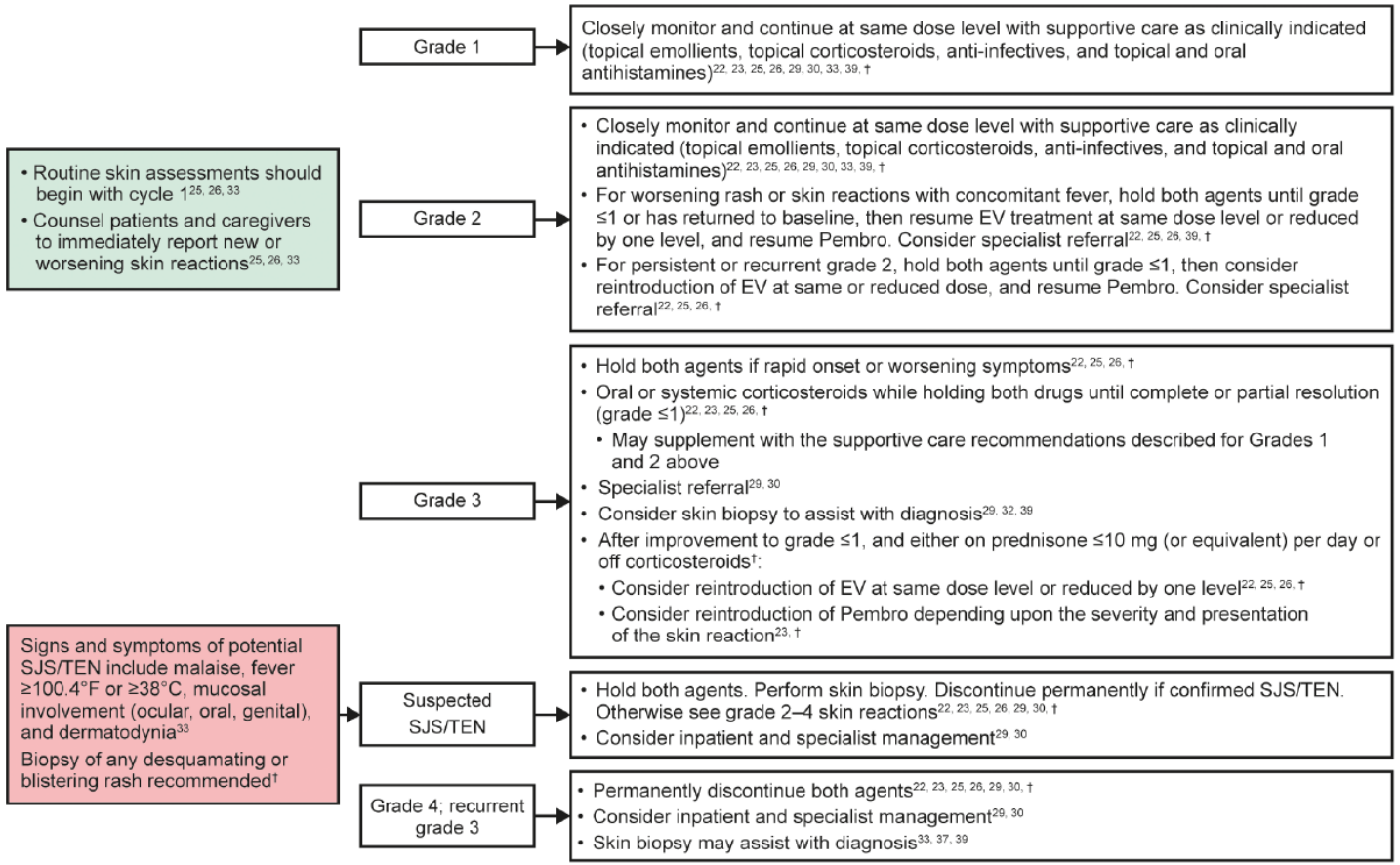
*Up to a maximum of 125 mg for patients weighing ≥100 kg.

AESI, adverse event of special interest; EV, enfortumab vedotin; EV+P, enfortumab vedotin plus pembrolizumab; SJS, Stevens–Johnson syndrome; SmPC, Summary of Product Characteristics; TEN, toxic epidermal necrolysis.

PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

Monitoring and management of skin reactions



Rash maculo-papular[2]
Grade 1: Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)
Grade 2: Macules/papules covering 10–30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL
Grade 3: Macules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADL

One adult palm is approximately equivalent to 1% of BSA. Therefore, 10% BSA corresponds to an area roughly equal to ten palm-sized regions

Images reproduced from 'Managing potential adverse events during treatment with enfortumab vedotin + pembrolizumab in patients with advanced urothelial cancer' Brower B et al. *Front Oncol* 2024;14:1326715. Available at: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2024.1326715/full. By CC: https://creativecommons.org/licenses/by-nc/4.0/.
ADL, activities of daily living; BSA, body surface area; EV, enfortumab vedotin; Pembro, pembrolizumab; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.
1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Available at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Last accessed: June 2025.

Summary

Severe skin toxicity can occur with EV+P, and requires proactive monitoring and management[1,2]

When rash occurs, close and frequent monitoring is necessary during the early phase to detect any signs of deterioration. Patients should be educated on the need to report changes[1,2]

EV+P is an effective treatment option for a broad patient population. Early identification and effective care can help ensure patients are able to continue to receive their treatment, to ensure patients receive optimal treatment outcomes[1,2]

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).

EV, enfortumab vedotin; P, pembrolizumab; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

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Genitourinary Masterclass

Best practice sharing: Practical approaches to patient care – Part 2

Professor Daniel Petrylak

Director of Genitourinary Oncology, Yale University Cancer Center, New Haven, USA

EV as first-line therapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer. Combination therapy with pembrolizumab.

EV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 or programmed death-ligand 1 inhibitor, and have received a platinum-containing chemotherapy

EV, enfortumab vedotin.
PADCEV® (enfortumab vedotin). Prescribing Information

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Patient case: Skin toxicity and peripheral neuropathy

- Male
- **Age: 72** years

Initial presentation

Gross hematuria

Further investigations

CT of abdomen/pelvis: Multiple lung nodules & 3 cm bladder mass

CT-guided biopsy of lung nodule: mUC

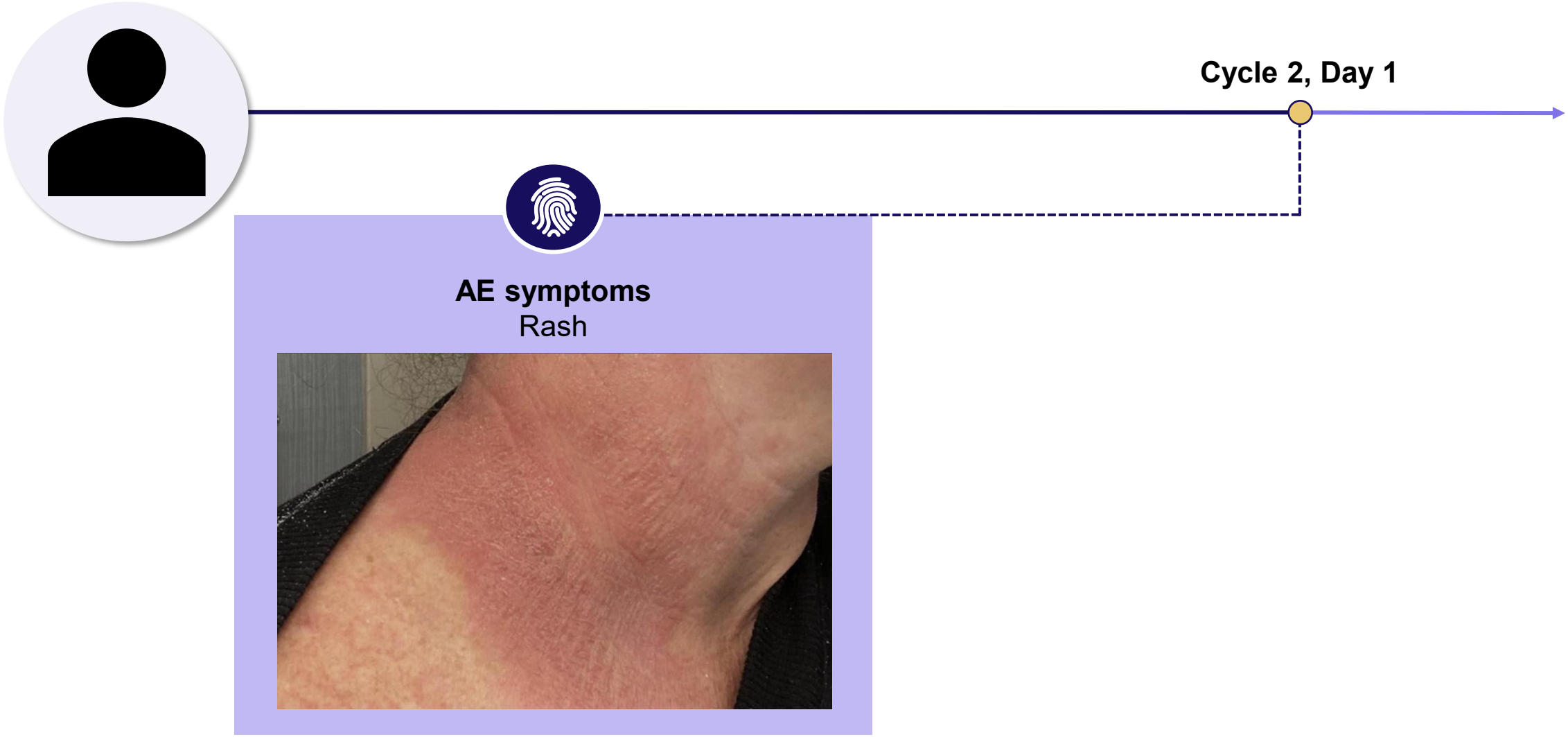
Chosen treatment

EV 1.25 mg/kg

Pembrolizumab 200 mg IVSS

CT, computed tomography; EV, enfortumab vedotin; IVSS, intravenous Soluset; mUC, metastatic urothelial carcinoma.

AE presentation and management: Skin toxicity [1/5]



AE, adverse event.

Question for the audience

What treatment would you use for this rash?

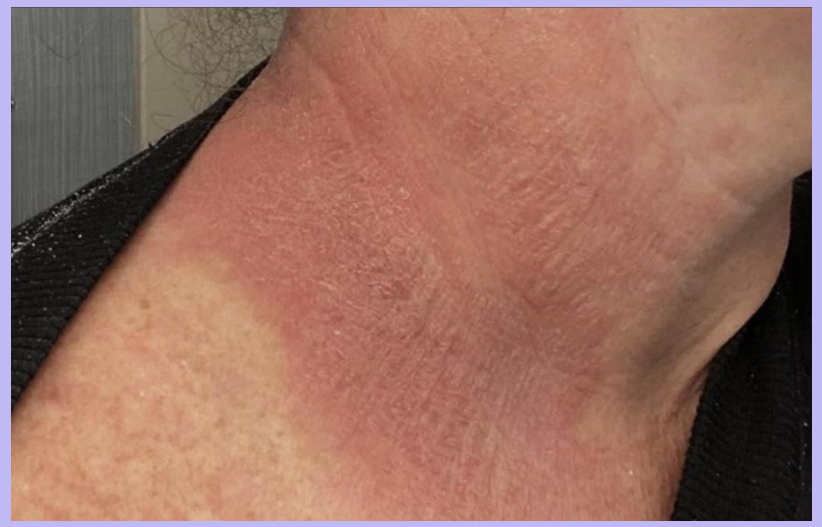
- **A** Topical steroids and continue treatment
- **B** Prednisone 40 mg PO QD and continue treatment
- **C** Hold EV, continue pembrolizumab
- **D** Hold EV, continue pembrolizumab, administer topical steroids

EV, enfortumab vedotin; PO, orally; QD, once daily.

AE presentation and management: Skin toxicity [2/5]

Cycle 2, Day 1

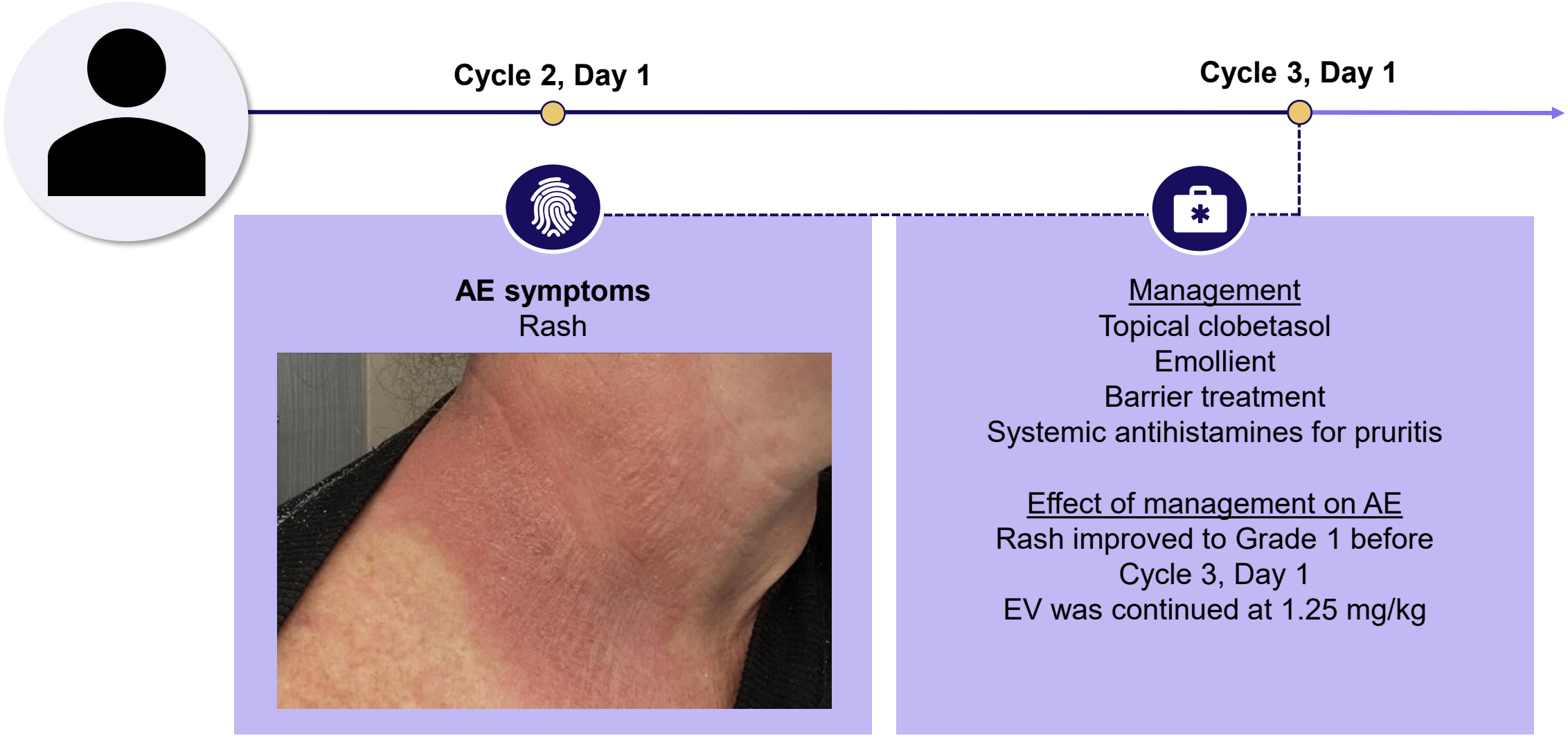
AE symptoms
Rash



<u>Management</u>
Topical clobetasol
Emollient
Barrier treatment
Systemic antihistamines for pruritis

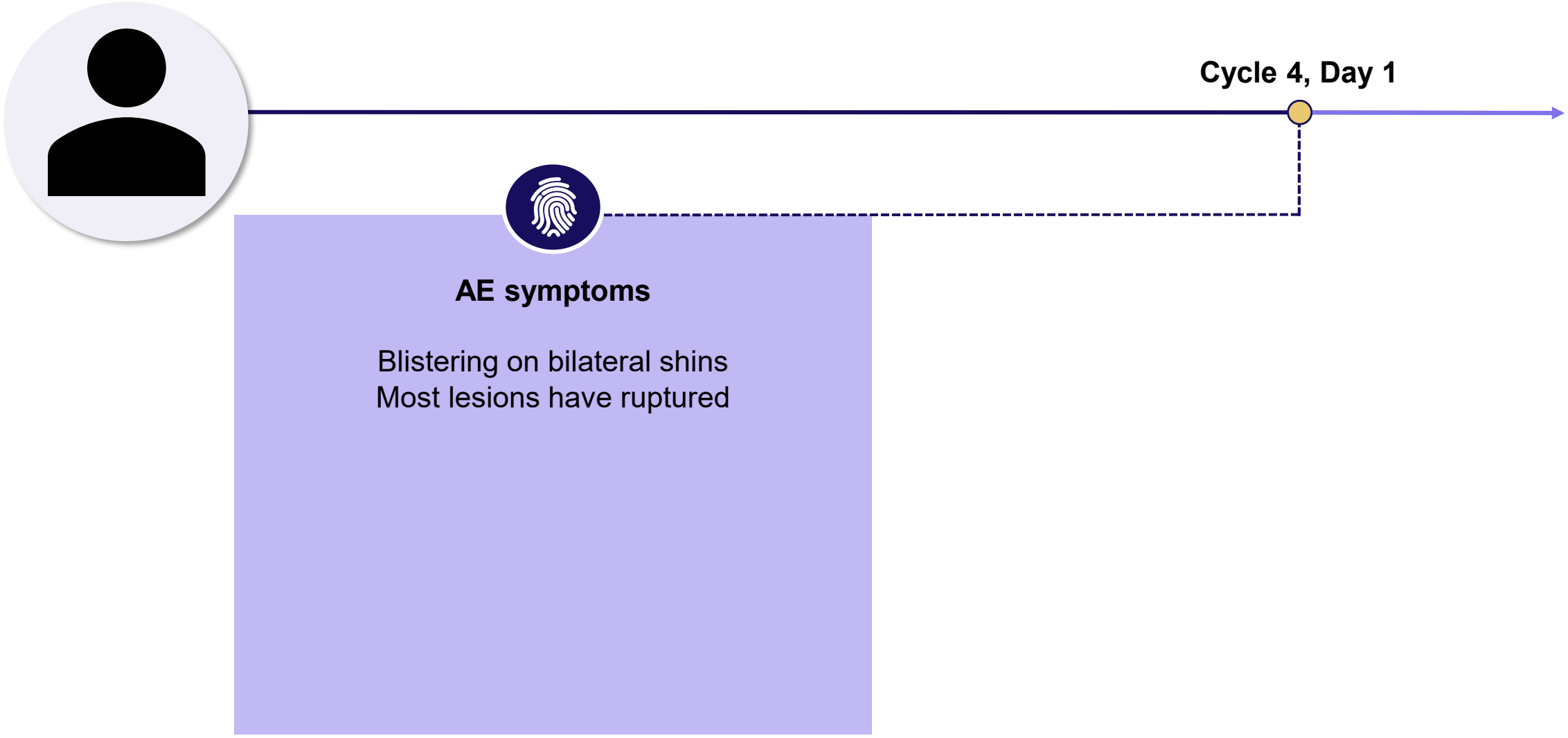
AE, adverse event.

AE presentation and management: Skin toxicity [3/5]



AE, adverse event; EV, enfortumab vedotin.

AE presentation and management: Skin toxicity [4/5]



AE, adverse event.

Question for the audience

What would you do next?

A. Systemic steroids, hold EV, continue pembrolizumab

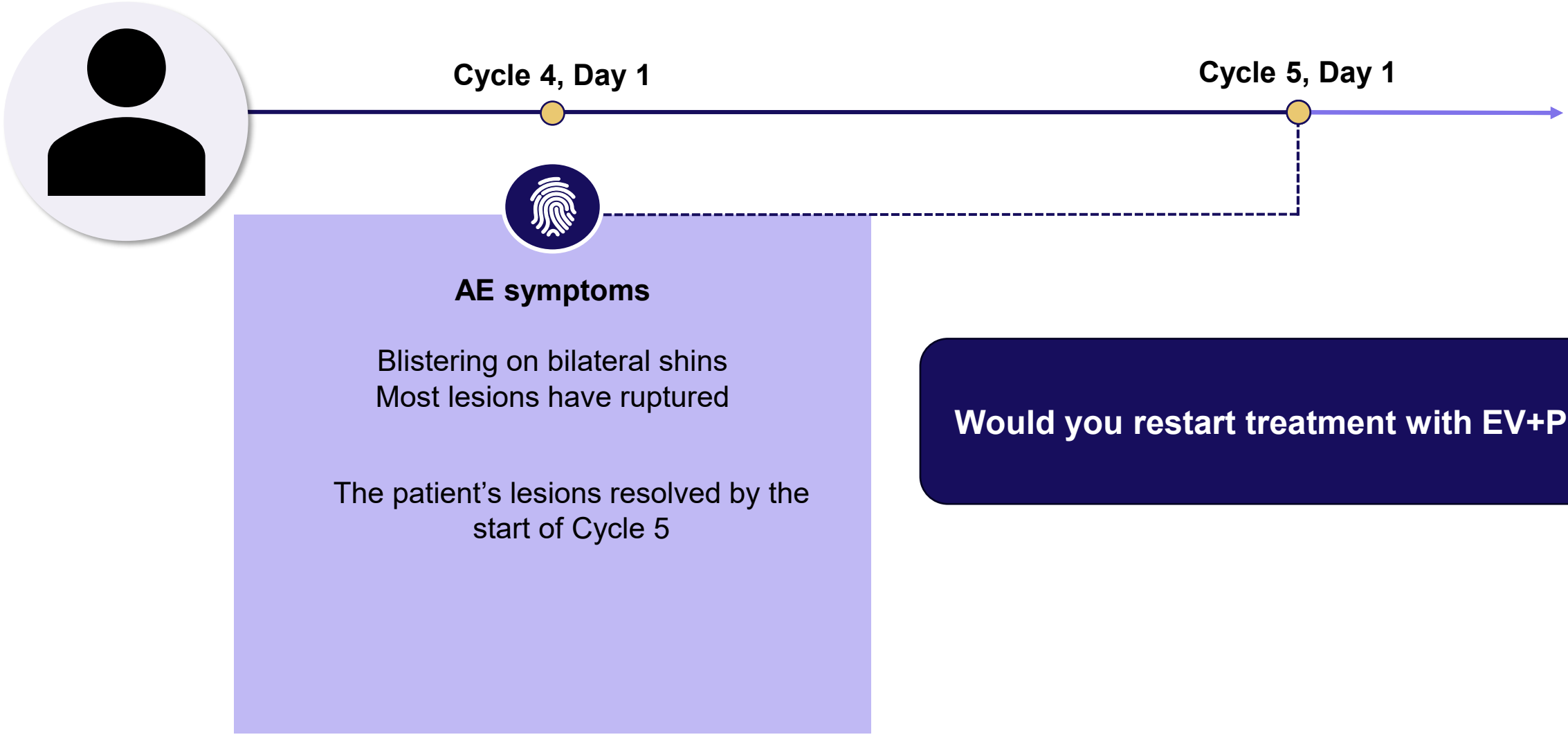
B. Systemic steroids, continue EV at 1.0 mg/kg, continue pembrolizumab

C. Continue EV 1.25 mg/kg and continue pembrolizumab

D. Systemic steroids, continue EV + pembrolizumab

EV, enfortumab vedotin.

AE presentation and management: Skin toxicity [5/5]



AE, adverse event; EV, enfortumab vedotin; P, pembrolizumab.

It is important we understand the safety profile of EV+P to stay ahead of AESIs

Skin toxicities[1,2]

Incidence: 70%
Grade ≥3: 17%

Severe skin reactions:[1]

1.7 months

Range: 0.1–17.2 months

Peripheral neuropathy[1–3]

Incidence: 63.2%
Grade ≥3: 6.8%

Grade ≥2:[3]

6 months

Range: 0.3–25 months

EV-302 trial exclusion criteria:[4]

Ongoing sensory or motor neuropathy Grade ≥2

Hyperglycemia[1–3]

Incidence: 13.0%
Grade ≥3: 8.9%

Any grade:[3]

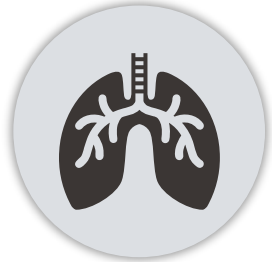
0.5 months

Range: 0.3–3.5 months

EV-302 trial exclusion criteria:[4]

Uncontrolled diabetes, defined as HbA_{1c} ≥8% or HbA_{1c} 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained

Pneumonitis/ILD[1,2]



Incidence: 10.3%
Grade ≥3: 3.5%*

Any grade:[1]

4 months

Range: 0.3–26.2 months

EV-302 trial exclusion criteria:[4]

History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis

Ocular AEs[1–3]

Incidence: 21.4%

EV-302 trial exclusion criteria:[4]

Active keratitis or corneal ulcerations

Median time to onset

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Skin toxicities: Risk factors and monitoring

Median time to onset of severe skin reactions:[3]

1.7 months

Most skin-related AEs are mild, transient, and occur early; however, they should still be reported and managed quickly to reduce the risk of progression to a more severe reaction, which may lead to EV+P treatment delays or discontinuation or even be fatal[1–3]

General risk factors for skin reactions to anti-cancer therapy[1,4]

Prior history of:

- Cutaneous reactions to previous anti-cancer therapies
- A dermatological condition
- Allergies
- Dry skin
- Immunosuppression
- Immune-mediated skin conditions
- A high level of sun exposure or radiation treatment
- Advanced age
- Renal and/or hepatic impairment

Patients receiving EV+P should be monitored for skin reactions at each clinic visit, including before each administration[1]

Complete visual inspection and palpation of the skin across the entire body[1,5]

Record and photograph the color, texture, morphology, distribution, and extent of lesions[5]

Monitor the skin for secondary skin infections[1]

Assess for presence of red flag symptoms (e.g., rash or itching that continues to get worse or comes back after treatment, skin blistering or peeling, mucosal involvement: Painful sores or ulcer in mouth or nose, throat, or genital area; fever or flu-like symptoms; and swollen lymph nodes[3]

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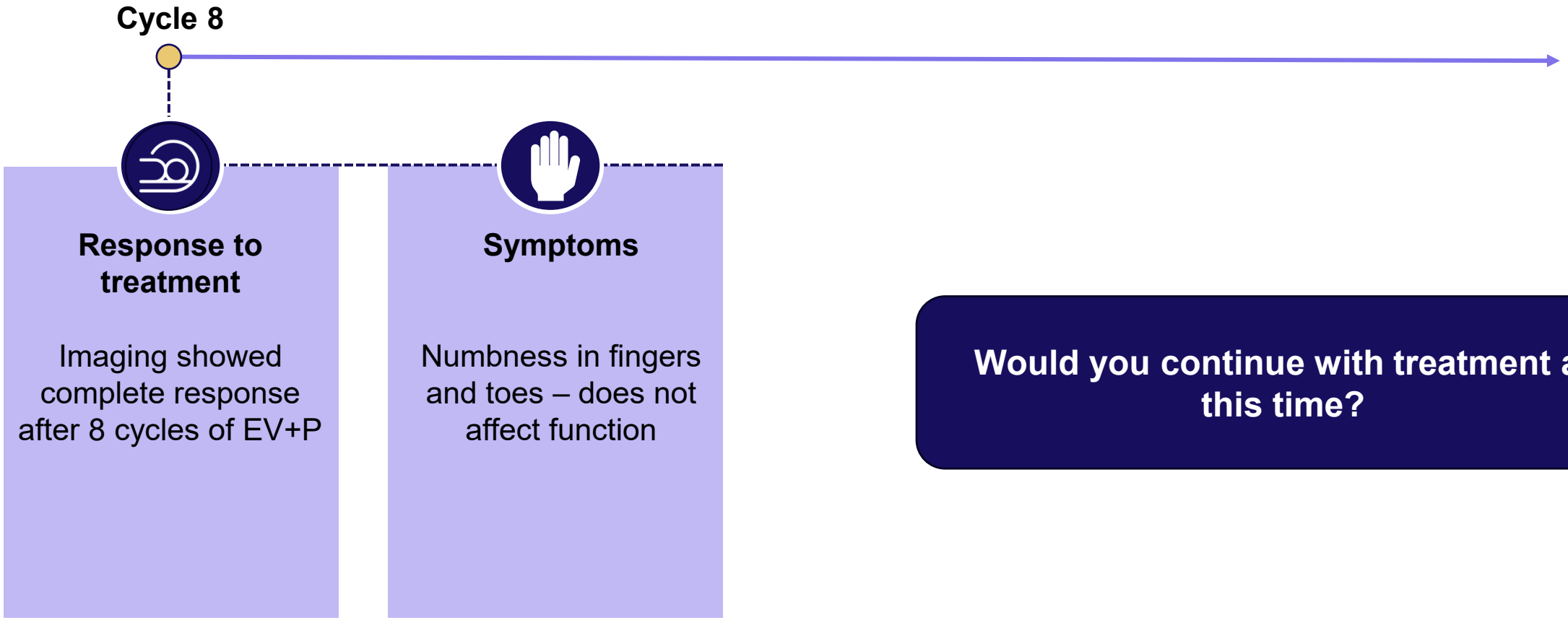
Response to treatment



Would you continue with treatment at this time?

EV, enfortumab vedotin; P, pembrolizumab.

PN: Risk factors and monitoring

Median time to onset of Grade ≥2 PN:[1]

6 months

PN is an AESI associated with EV, though it may also occur with P.[1,2] In the EV-302 trial, **63.2% of patients developed EV-related PN, of which 6.8% developed Grade ≥3 PN**[2,3]

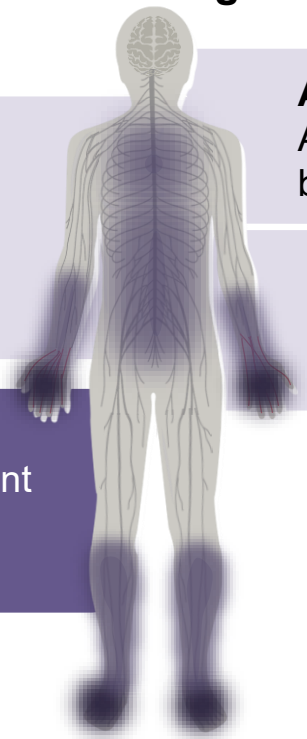
General risk factors[4,5]*

- Pre-existing neuropathy
- Uncontrolled diabetes mellitus
- Pre-existing infection (e.g., HIV)
- Age (≥75 years)
- Family history of neuropathy
- Spinal involvement of mUC
- Non-malignant spinal disease
- Liver/thyroid/kidney disorders
- Autoimmune disease
- Vitamin deficiency
- Smoking
- Increased BMI
- Alcohol abuse

Screening questions for PN are recommended at each visit for patients receiving EV+P treatment,[1] as PN results from damage caused by anti-cancer therapies[5]

Sensory effects[4]
Typically affect hands and feet

Autonomic effects[4]
Affect involuntary bodily processes



Motor effects[4]
Can progress from sensory effects

Conduct functional assessment of fine motor skills: Observe patient buttoning, zipping, or threading a needle[5]

Conduct functional assessment of gait and balance and assess lower-extremity strength and sensation[5]

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*In addition to exposure to neurotoxic agents, such as anti-cancer therapies.[1]

AESI, adverse event of special interest; BMI, body mass index; EV, enfortumab vedotin; HIV, human immunodeficiency virus; mUC, metastatic urothelial carcinoma; P, pembrolizumab; PN, peripheral neuropathy.

1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. Powles T et al. *N Engl J Med* 2024;390:875–888 (supplementary appendix); 3. Powles T et al. *N Engl J Med* 2024;390:875–888;
4. Jordan B et al. *Ann Oncol* 2020;31:1306–1319; 5. Pace A et al. *Clin J Oncol Nurs* 2021;25.

SmPC management guidance

AESI	Severity	Dose modification
Peripheral neuropathy	**Grade ≥3**	Permanently discontinue
	Grade 2	• Withhold until Grade ≤1 • For first occurrence, resume treatment at the same dose level • For a recurrence, withhold until Grade ≤1, then resume treatment reduced by one dose level

Dose reduction schedule

Starting dose
1.25 mg/kg*
up to 125 mg

First dose reduction
1.00 mg/kg
up to 100 mg

Second dose reduction
0.75 mg/kg
up to 75 mg

Third dose reduction
0.50 mg/kg
up to 50 mg

*Up to a maximum of 125 mg for patients weighing ≥100 kg.
AESI, adverse event of special interest; SmPC, Summary of Product Characteristics.
PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

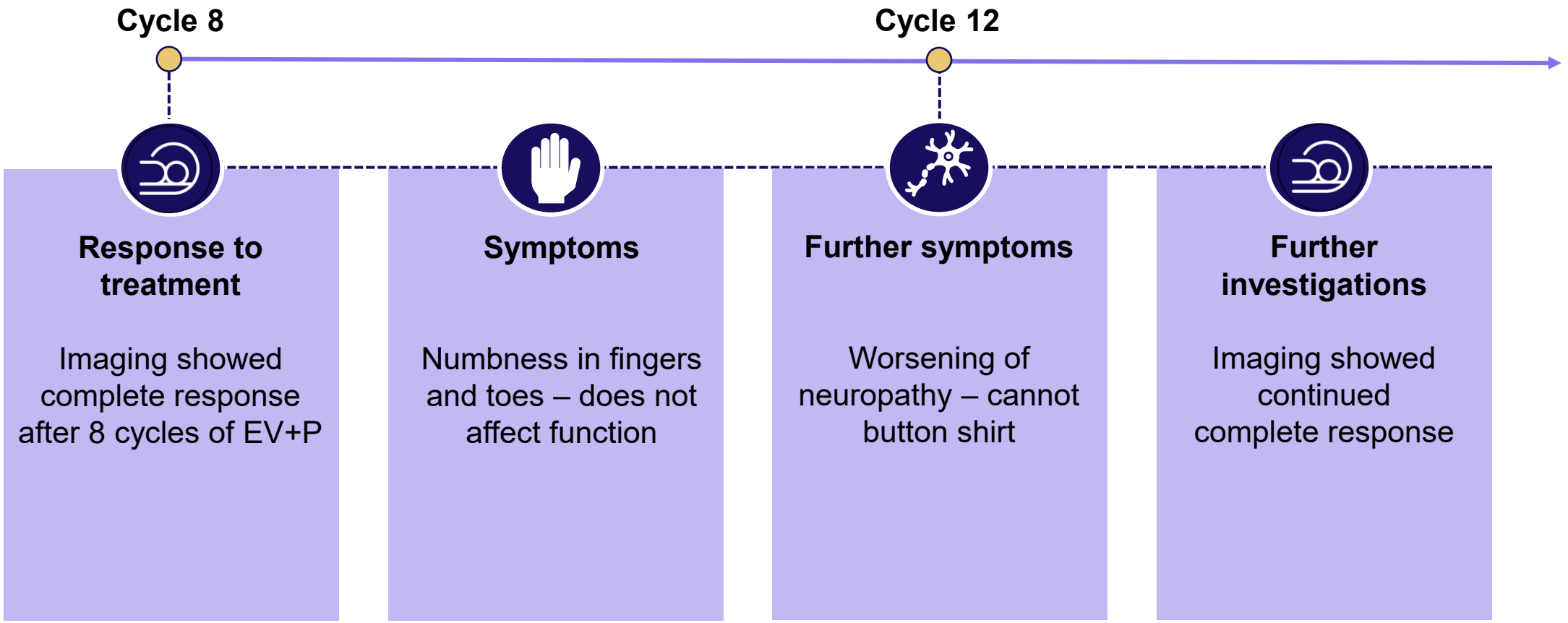
Question for the audience

What would you do next?

- A Reduce dose of EV to 1.0 mg/kg
- B Hold EV, then resume at reduced dose
- C Hold EV, then resume at full dose
- D Continue at same dose

EV, enfortumab vedotin.

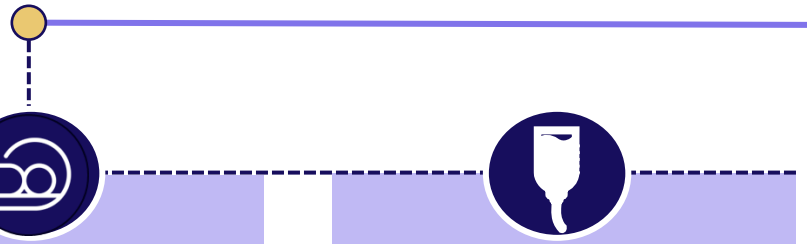
Response to treatment and peripheral neuropathy



EV, enfortumab vedotin; P, pembrolizumab.

Response to treatment and management of peripheral neuropathy

4 months after Cycle 12



Intervention

Neuropathy improved to Grade 2 after a 4-month treatment break

Response

Patient remains in complete response

Would you restart treatment at this time?

Summary

Severe skin toxicity can occur with EV+P, and requires proactive monitoring and management[1,2]

When rash occurs, close and frequent monitoring is necessary during the early phase to detect any signs of deterioration. Patients should be educated on the need to report changes[1,2]

PN is a frequent, dose-limiting toxicity associated with EV use; however, early recognition of treatment-emergent PN and prompt intervention with the use of dose modifications provides the best chance for resolution, without impacting the ability to maintain response to EV[1]

EV+P is an effective treatment option for a broad patient population. Early identification and effective care can help ensure patients are able to continue to receive their treatment, to ensure patients receive optimal treatment outcomes[1,2]

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Best-practice sharing: Practical approaches to patient care – Part 2

Dr. Jiun-I Lai

Division of Medical Oncology, Department of Oncology, Veterans General Hospital, Taipei, Taiwan

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EV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 or programmed death-ligand 1 inhibitor and have received a platinum-containing chemotherapy.

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Case 2
Introducing – Ms. L

Ms. L

- Taiwanese female
- **Age: 72** years
- **ECOG PS: 0**
- **GFR: 51** mL/min
- **BMI: 13.1** kg/m^2
- **HbA1c: 5.8** mmol/mol (%)

Lifestyle: Sedentary

Employment status/job: Retired

Family history of cancer: None

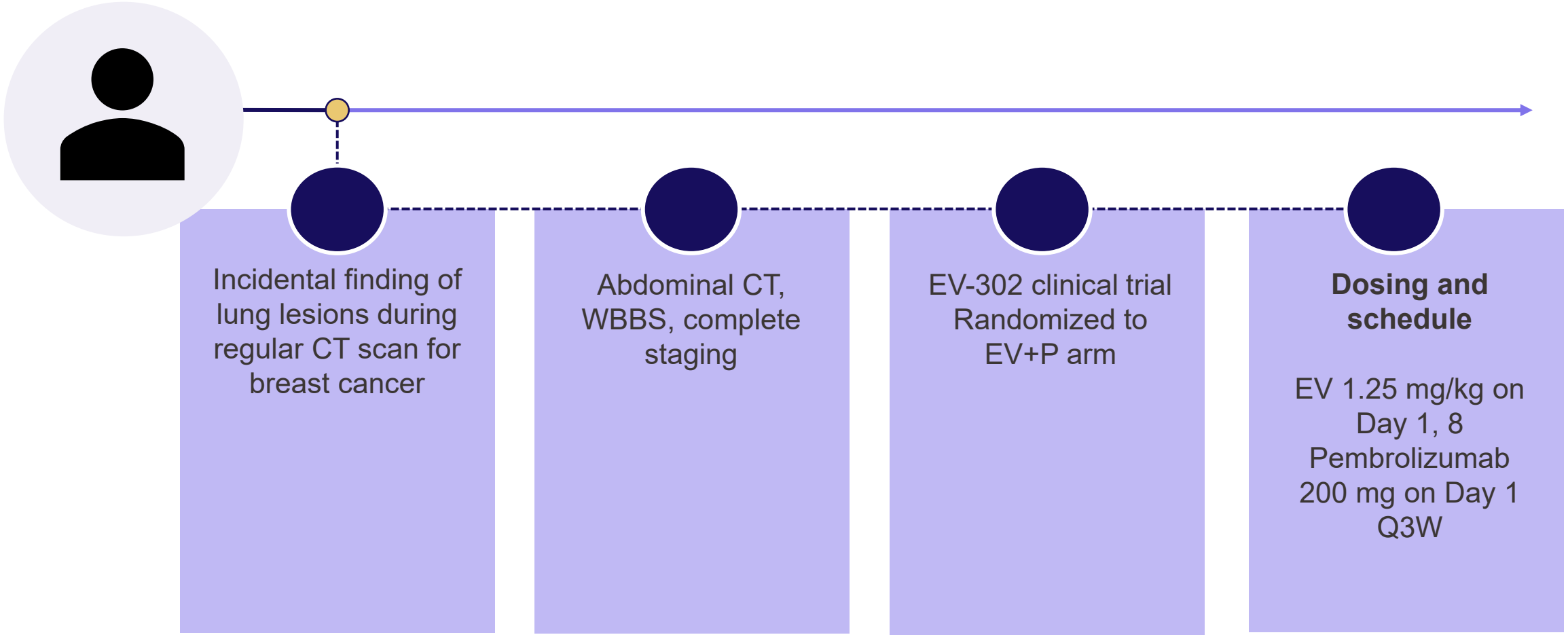
Comorbidities: none

Concomitant medications: HTN

Any other relevant medical history: Stage 2 breast cancer, completed adjuvant chemotherapy, resected 6 years ago, on Femara for 6 years

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin.

Diagnosis, treatment initiation, dosage, and schedule



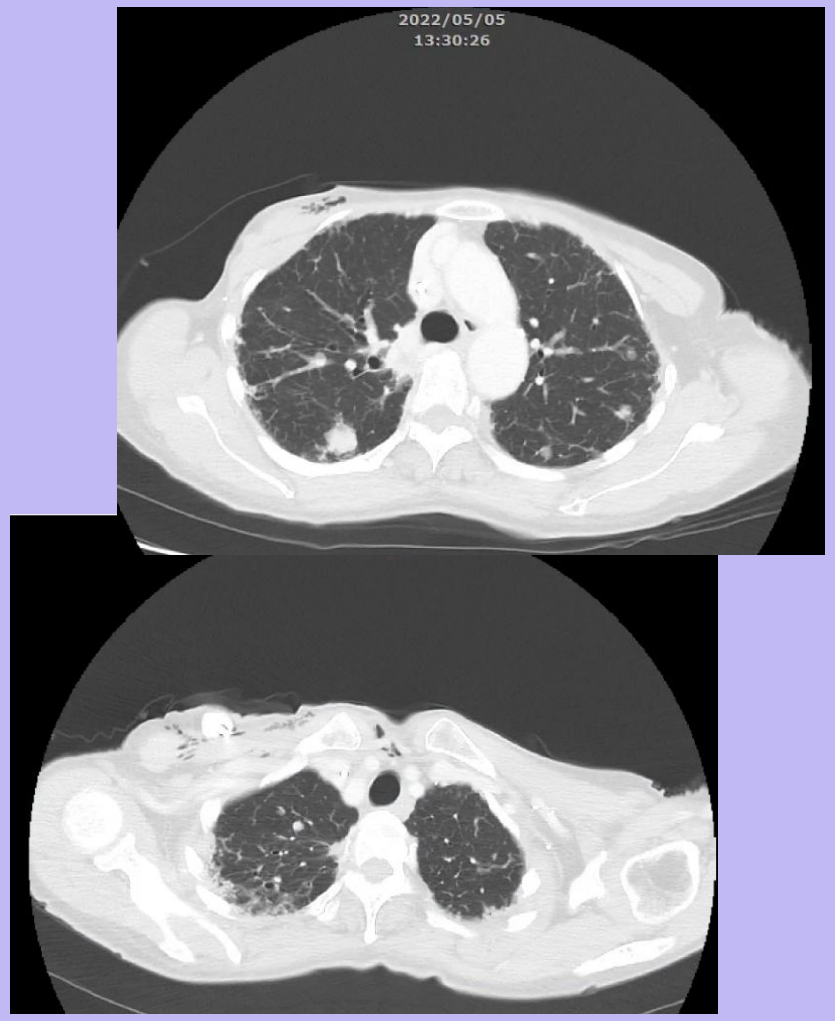
CT, computed tomography; EV, enfortumab vedotin; P, pembrolizumab; Q3W, every 3 weeks; WBBS, whole-body bone scanning.

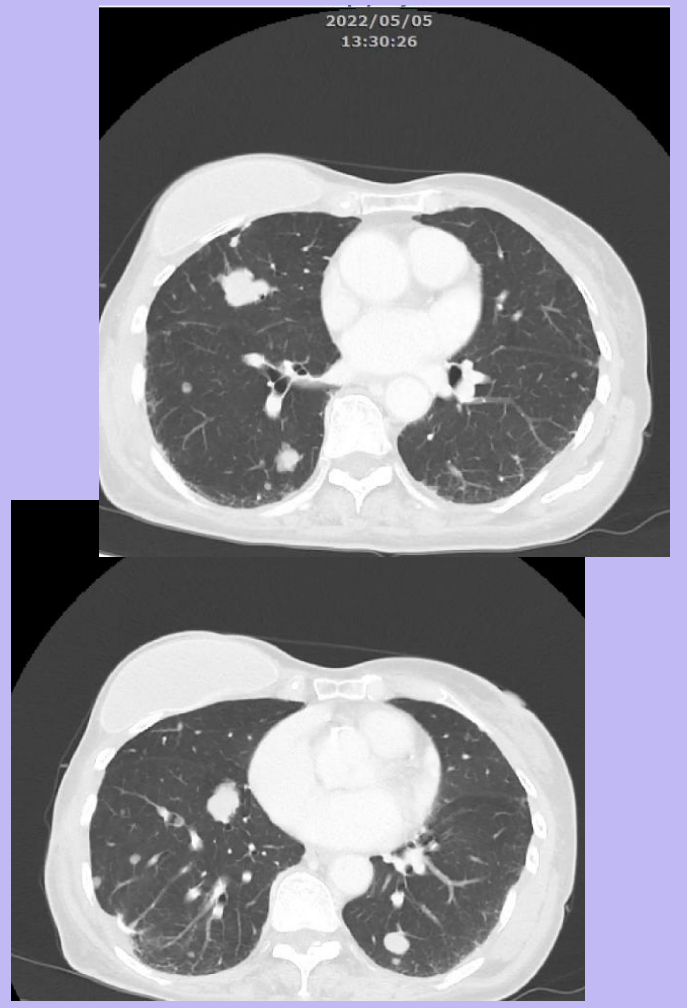
Imaging workup – May 2022

- Chest CT
  - Bilateral lung parenchyma: Multiple ill-defined nodular lesions were noted in bilateral lung fields, compatible with lung metastasis (S/I 2/35, 2 cm in RML; S/I 2/41, 2 cm in RLL)
  - Mediastinal lymph node: No definite enlarged lymphadenopathy
- Abdominal CT
  - Kidney: Soft tissue in left upper ureter with severe hydronephrosis, compatible with urothelial carcinoma
  - Mild dilatation of the left middle ureter, cannot R/O stenosis/tumor infiltration in left lower ureter
  - Lymph node: Enlarged lymph node was noted at left para-aortic region (S/I 4/37, 2.4×1.2 cm) and aortocaval region (S/I 4/31, 2.0×1.6 cm), in favor of metastatic lymphadenopathy

.
CT, computed tomography.

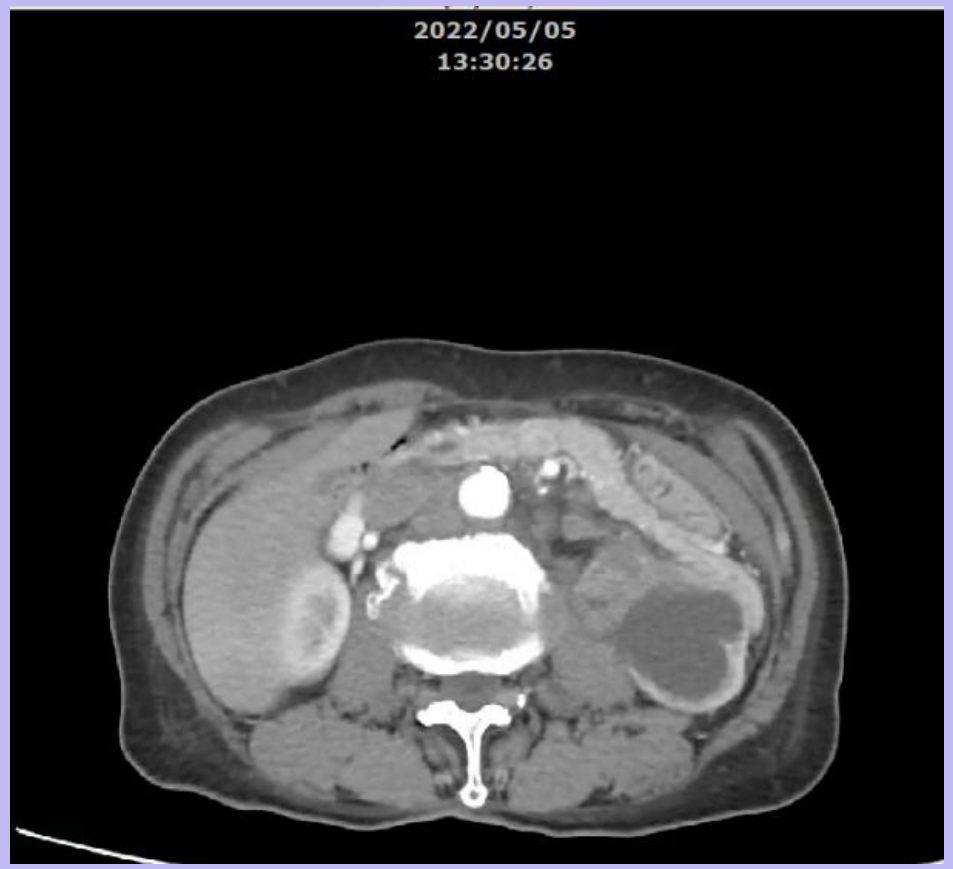
Treatment response

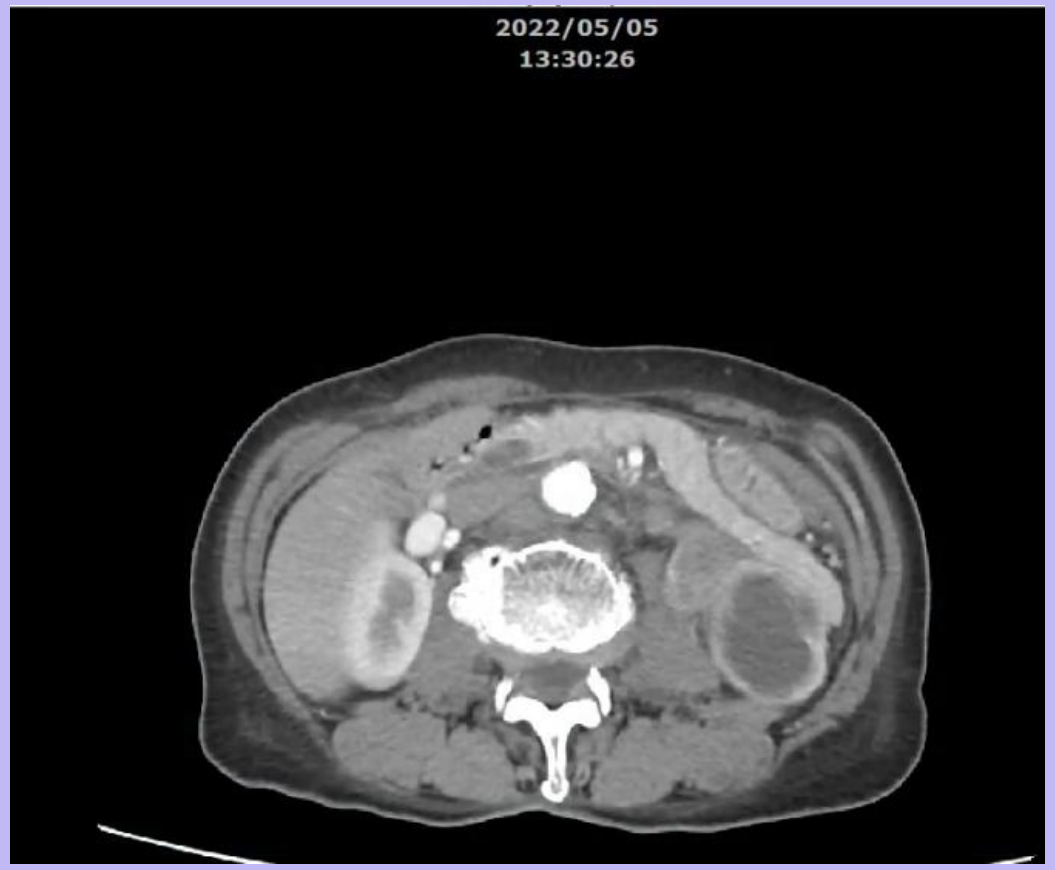




Images courtesy of Dr. Jiun-I Lai with permission of the patient.

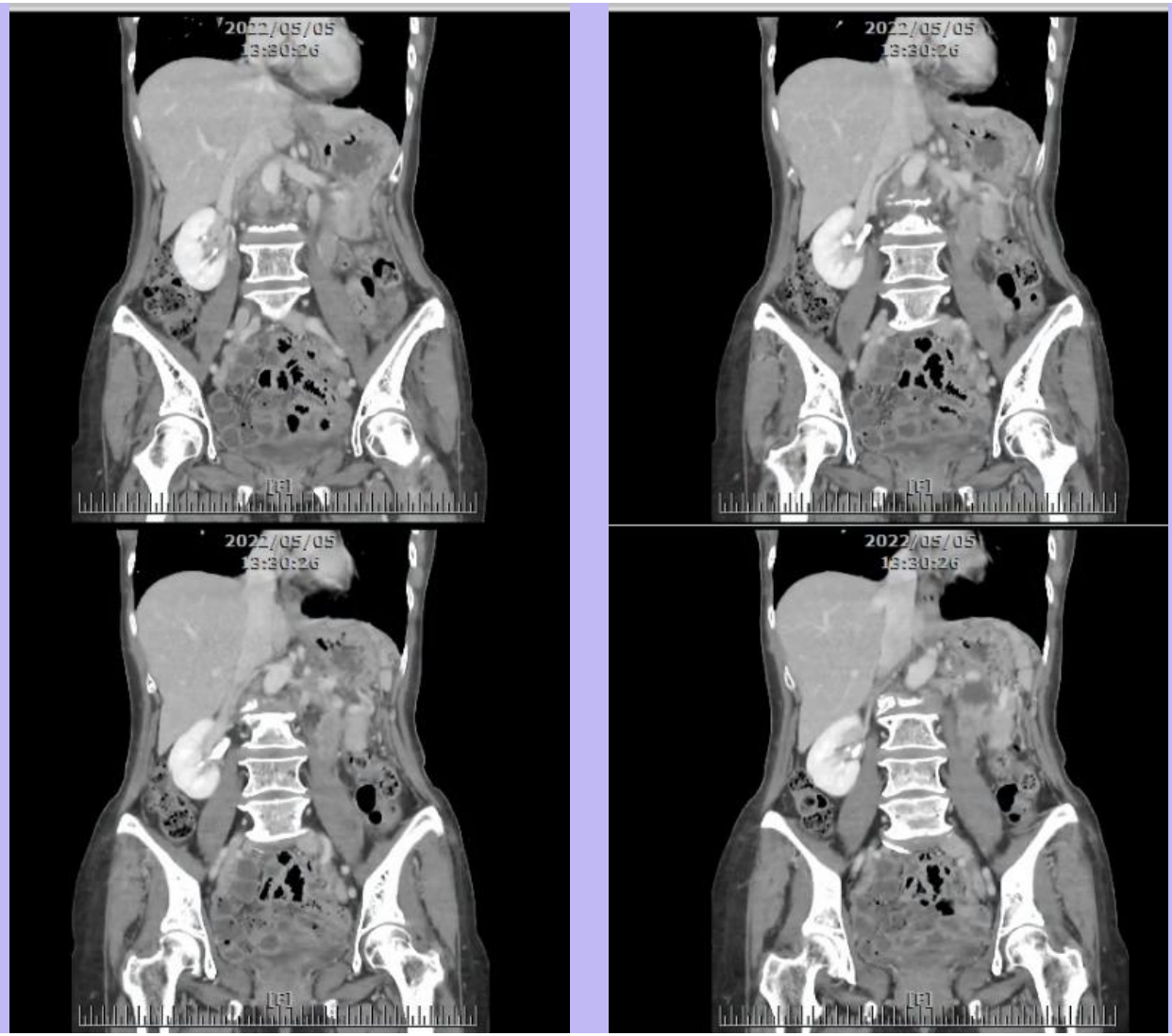
Treatment response





Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



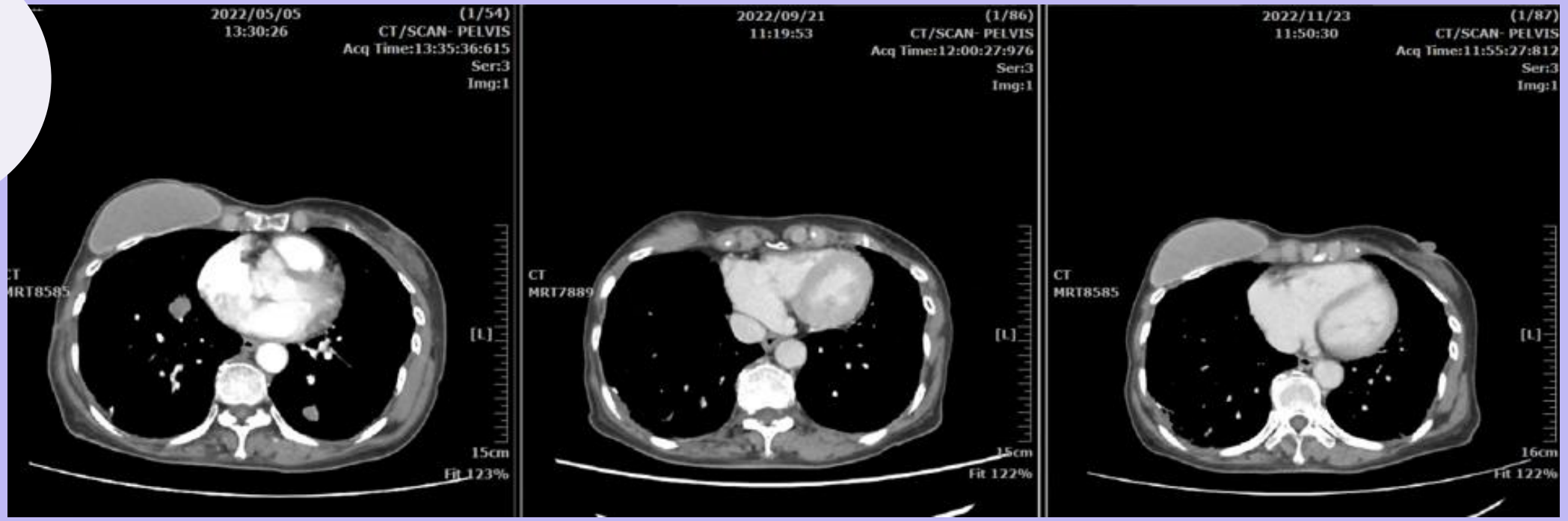
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Diagnosis and treatment

- Diagnosis: Left UTUC with lung and lymphadenopathy metastases, T4N2M1
- Started on EV+P (EV-302) trial protocol since 2022/5/19

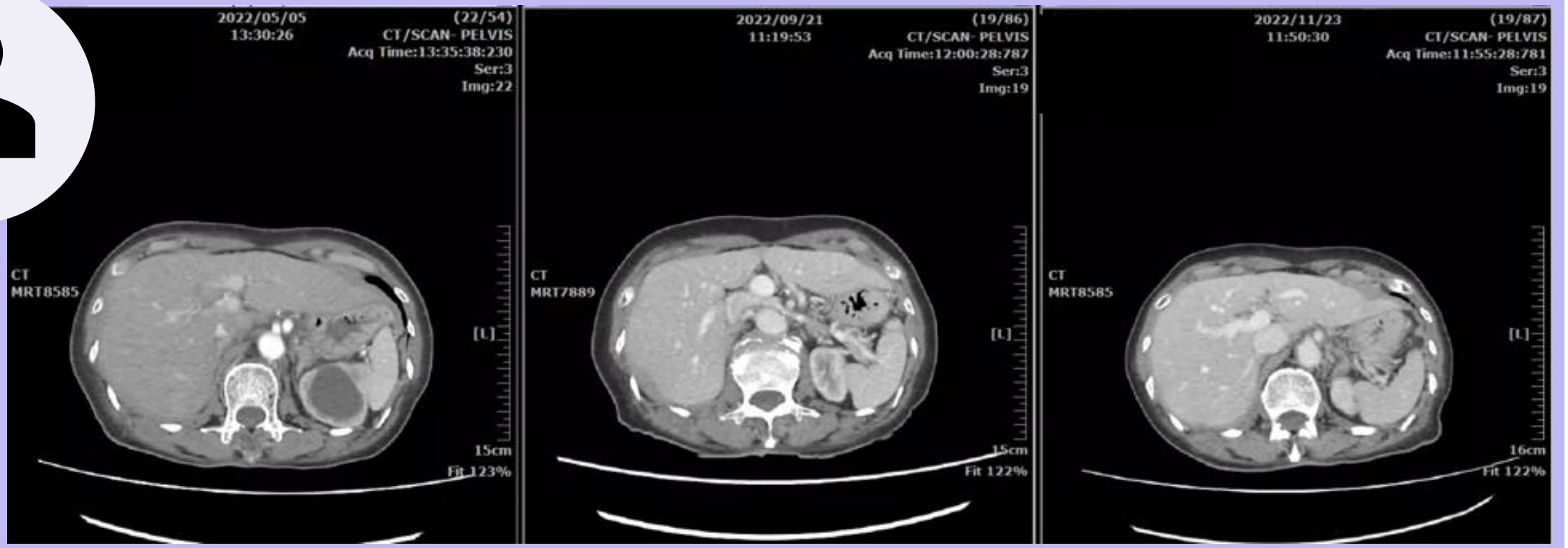
EV, enfortumab vedotin; P, pembrolizumab; UTUC, upper urinary tract urothelial carcinoma.

Treatment response



Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Treatment response



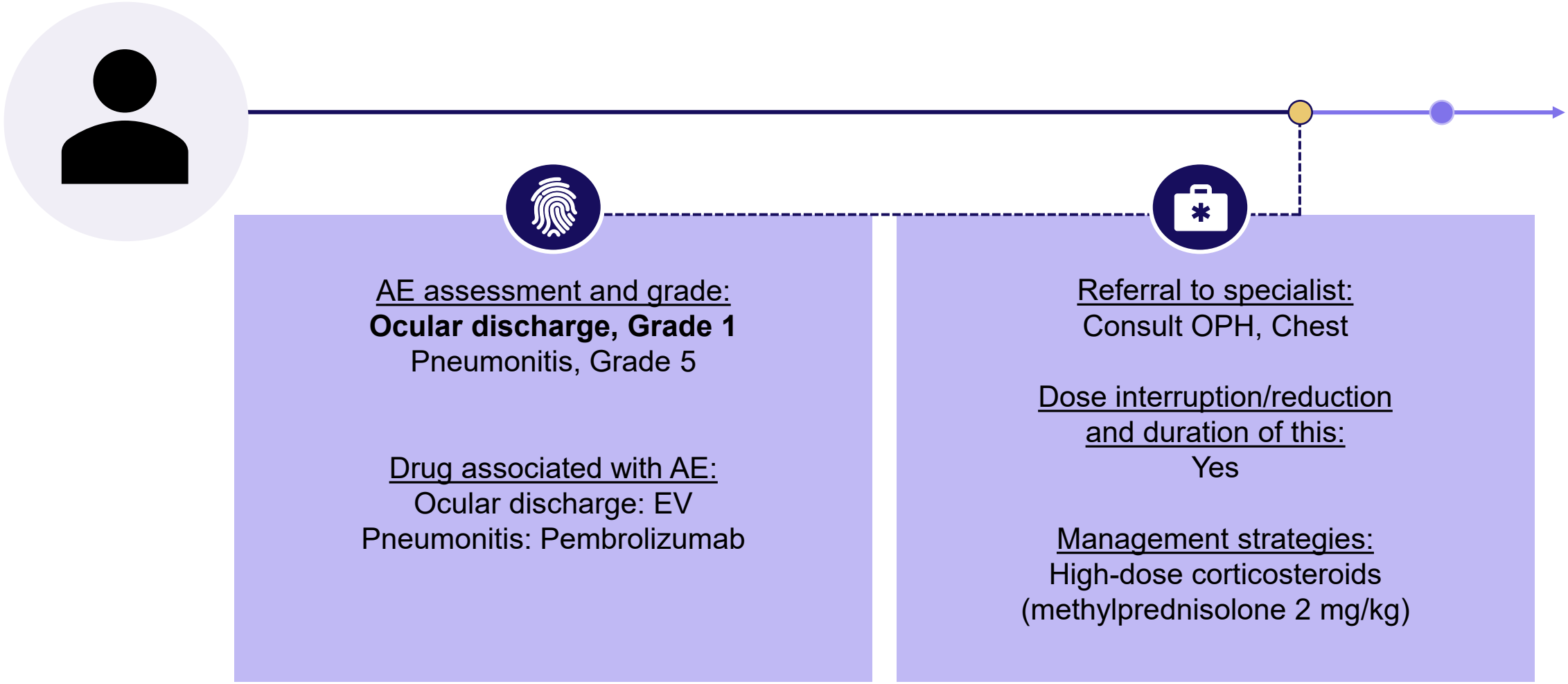
Images courtesy of Dr. Jiun-I Lai with permission of the patient.

Diagnosis and treatment

- Diagnosis: Left UTUC with lung and lymphadenopathy metastases, T4N2M1
- Started on EV+P (EV-302) trial protocol since 2022/5/19
- Achieved near CR in most lesions after 4 months of initiating treatment and remained durable response until 20 months

CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; UTUC, upper urinary tract urothelial carcinoma.

AE presentation and management



AE, adverse event; EV, enfortumab vedotin; OPH, ophthalmology.

Ocular AEs in EV clinical trials

Trial	Ocular AE incidence (any grade)	Dry eye (any grade)	Grade 3/4 ocular AE	Notes
EV-301 (EV monotherapy)[1]	15.9% (dry eye), 4.1% (blurred vision), 0.7% (corneal disorders)	15.9% (dry eye)	0.7% (Grade 3 dry eye)	Median onset of dry eye 1.7 months[2]
EV-302 (EV+P)[3]	21.4% (ocular disorders overall)	18.6% (dry eye)	0	Combination EV + pembrolizumab;[3] generally mild[4]

AE, adverse event; EV, enfortumab vedotin.

1. Powles T, et al. *N Engl J Med* 2021;384:1125–1135 (supplementary); 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 3. Powles T, et al. *N Engl J Med* 2024;390:875–888 (supplementary); 4. Speaker's own opinion.

Blepharitis: inflammation of the eyelid[1,2]

- Blepharitis is chronic ocular inflammation primarily involving the eyelid margin, found in approximately 47% of patients presenting for eye examinations[1]
- Eyelid Margin: this is the area where the eyelid meets the eye
- Eyelashes (Cilia): located on the anterior margin
- Meibomian glands: these are modified sebaceous glands located within the tarsal plates of the eyelids. there are about 25-40 in the upper lid and 20-30 in the lower lid. They secrete meibum, an oil that forms the lipid layer of the tear film, preventing tear evaporation. Their openings are on the posterior eyelid margin
- Glands of Zeis and Moll: these are smaller glands associated with the **eyelashes**
- Glands of Zeis: sebaceous glands that produce oil
- Glands of Moll: modified sweat glands
- Conjunctiva: a thin, transparent membrane that lines the inside of the eyelids (palpebral conjunctiva) and covers the white part of the eye (bulbar conjunctiva)

1. Lemp MA, et al. *The Ocular Surface* 2009;7:S1–S14; 2. Speaker's own opinion.

Blepharitis: inflammation of the eyelid[1,2]

- Anterior Blepharitis:
  This affects the outside front edge of the eyelid, where the eyelashes are attached
  - Staphylococcal blepharitis: often caused by an overgrowth of bacteria, particularly Staphylococcus aureus
  - Seborrheic Blepharitis: strongly associated with seborrheic dermatitis (dandruff of the scalp and eyebrows)
- Posterior Blepharitis:
  This is the most common cause of posterior blepharitis and a **primary contributor to dry eye disease**
  The glands become blocked with thick, waxy secretions, leading to:
  - reduced lipid secretion into the tear film
  - increased tear evaporation and tear hyperosmolarity
  - unstable tear film, causing dry eye symptoms
  - favorable environment for bacterial growth

1. Speaker's own opinion; 2. Arrúa M et al. Arch Soc Esp Oftalmol 2015;90:112–118.

Link between blepharitis and EV

- FDA label for EV associated ocular events includes:[1]
  - **Blepharitis**, **conjunctivitis**, conjunctivitis allergic, corneal abrasion, corneal degeneration, corneal erosion, corneal toxicity, **dry eye**, exposure keratitis, eye irritation, keratitis, keratoconus, lacrimation increased, **meibomian gland dysfunction**, ocular discomfort, punctate keratitis, vision blurred, visual acuity reduced, visual impairment
- High prevalence of ocular adverse events also noted with tisotumab vedotin: 53% of patients using TV had ocular adverse effects, with 23% dry eye[2]
- Case reports have described association between blepharitis and various ADCs[3]

ADC, antibody-drug conjugate; EV, enfortumab vedotin; FDA, U.S. Food and Drug Administration.

1. Brave MH, et al. *Clin Cancer Res* 2024;30:4815–4821; 2. Lent-Schochet D, et al. *Gynecologic Oncology Reports* 2025;57:101676; 3. Speaker's own opinion.

Treatment for ADC-associated ocular side effects[1]

Preservative free artificial tears	Lubricates the ocular surface and promotes healing. The preservatives in some artificial tears can be irritating to the ocular surface, and, therefore, preservative free options are preferred.
Vitamin A ointment	Promotes wound healing, helps treat ocular keratinization, and provides lubrication.
Insulin drops	Promotes corneal healing in severe dry eye or persistent epithelial defects.
Antibiotic drops or ointments	Prevents or treats infection.
Culture of ocular surface	Helps direct treatment of infectious conjunctivitis or keratitis.
Topical steroids	Reduces ocular surface inflammation. Should generally be avoided if there is concern for infection.
Amniotic membrane	Avascular fetal membrane that is used to promote healing of the ocular surface.
Oral Vitamin C	Promotes wound healing and reduces inflammation.
Oral doxycycline	Inhibits collagen breakdown. Also inhibits matrix metalloproteinases 2 and 9, as well as interleukin-1, to promote corneal healing.
Pseudomembrane debridement	Removal of pseudomembranes (membrane-like plaques of fibrinous inflammatory exudate) from the ocular surface can aid diagnosis (e.g. culture/pathology), improve comfort, and hasten ocular surface healing.

Guidance for EV:[2,3]

- Monitor patients for ocular disorders
- Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve
- Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam
- Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders

HCPs should refer to local SmPC guidance.

ADC, antibody-drug conjugate; EV, enfortumab vedotin; FDA, U.S. Food and Drug Administration.

1. Lent-Schochet D, et al. *Gynecologic Oncology Reports* 2025;57:101676; 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 3. Speaker's own opinion.

Question for the audience

How would you manage EV-related Grade 1 ocular discharge?

- **A** Artificial tears
- **B** Maintain EV dose and treat discharge
- **C** Permanently discontinue EV
- **D** Other

Footnotes

Question for the audience

How would you manage this adverse event?

- A **Artificial tears**
- B **Maintain EV dose and treat discharge[1]**
- C **Permanently discontinue EV**
- D **Other**

Footnotes

Baseline ophthalmology visit (2022/5/5)

```
VA: 0.05x1/3sc 6/60cgl 6/15cc OD, 0.05x1/3sc 6/30cgl 6/12cc OS
IOP: 16/16mmHg
1110505 ref: -12.25-1.75x80/-12.25-1.0x90
conj: mild congestion ou,cornea: clear ou
AC: deep silent ou, lens: NS+ou
Fd: C/D 0.4x0.5 od, 0.6x0.6 os
1110505 OCT:normal macular contour
```

- High myopia with astigmatism
- Subnormal best corrected visual acuity, likely due to early cataract (NS+) or myopic changes
- Normal IOP
- Mild conjunctival redness
- Slightly enlarged C/D ratio on the left may need glaucoma monitoring
- Macula seems to be normal on OCT

Second ophthalmology visit (2022-7)

```
VA: 0.05x1/3sc 6/60cgl 6/15cc OD, 0.05x1/3sc 6/30cgl 6/12cc OS
IOP: 16/16mmHg
1110505 ref: -12.25-1.75x80/-12.25-1.0x90
Blepharitis,bil with increaed tear lake,OU mucoid discharge,OS>OD  bulbar
conjunctiva not injected,OS but mucoid discharge with macerated skin over
temp side=> add GMO
conj: mild congestion ou,cornea: clear ou
AC: deep silent ou, lens: NS+ou
Fd: C/D 0.4x0.5 od, 0.6x0.6 os
1110505 OCT:normal macular contour
```

Drugs given:
Chloramphenicol "K" oph *sol 5 mL -
Flucason oph * susp. 0.02% 5 mL -
GENTAMICIN "K.D."OPH *OINT0.3%5G

Category	Previous note	Current note (image)	Change
VA (visual acuity)	OD: 6/60 cgl → 6/15 cc OS: 6/30 cgl → 6/12 cc	Same	**No change**
IOP	16/16 mmHg	Same	**No change**
Refraction	-12.25 -1.75×80 -12.25 -1.00×90	Same	**No change**
Conjunctiva	Mild congestion OU	More detailed: - OU mucoid discharge - OS > OD - OS macerated skin - OU not injected	**Worsened signs of blepharitis**
Cornea	Clear OU	Same	No change
Lens	NS+ OU	Same	No change
Anterior chamber (AC)	Deep silent OU	Same	No change
Fundus (Fd)	C/D: 0.4×0.5 OD 0.6×0.6 OS	Same	No change
OCT	Normal macular contour	Same	No change
New diagnosis	Not mentioned	Blepharitis bil (both eyes), tear lake ↑, mucous discharge, skin maceration OS	**New clinical issue added**
Plan/Treatment	Not mentioned	“Add GMO” (likely artificial tears or eye ointment like Genteal or GenTeal Moisturizing Ointment)	**Treatment plan added**

bil, bilateral; C/D, cup-to-disc; IOP, intraocular pressure; NS, nuclear sclerosis; OCT, optical coherence tomography; OD, right eye; OS, left eye; OU, both eyes.

Third ophthalmology visit (2022-8)

```
VA: 0.05x1/3sc 6/60cgl 6/15cc OD, 0.05x1/3sc 6/30cgl 6/12cc OS
IOP: 15/14(N, topcon) mmHg
1110505 ref: -12.25-1.75x80/-12.25-1.0x90
Blepharitis,bil with increaed tear lake,OU mucoid discharge,OS>OD  bulbar
conjunctiva not injected,OS but mucoid discharge with macerated skin over
temp side=> add GMO
conj: mild congestion ou,cornea: clear ou
AC: deep silent ou, lens: NS+ou
Fd: C/D 0.4x0.5 od, 0.6x0.6 os
1110505 OCT:normal macular contour
```

Drugs given:
Flucason oph * susp. 0.02% 5 mL -

Change dressing for the discharge

Afterwards, no more OPH clinic visit, Occasionally ask for eye drops and topical steroids at oncology clinic

Category	Status	Category	Status
Visual acuity	Stable	Visual acuity	Stable
Eye pressure	Slight decrease, normal	Eye pressure	Slight decrease, normal
Refraction	No change	Refraction	No change
Lens (cataract NS+)	Stable	Lens (cataract NS+)	Stable
New problem	**Blepharitis with mucous discharge, OS > OD**	**New problem**	**Blepharitis with mucous discharge, OS > OD**
Conjunctiva	**Worsened OS**	Conjunctiva	**Worsened OS**
Fundus and OCT	Stable	Fundus and OCT	Stable
Category	Status	Category	Status
Visual acuity	Stable	Visual acuity	Stable
Eye pressure	Slight decrease, normal	Eye pressure	Slight decrease, normal
Refraction	No change	Refraction	No change

NS, nuclear sclerosis; OCT, optical coherence tomography; OD, right eye; OPH, ophthalmology; OS, left eye.

Clinical course

- Started on EV+P in 2022-5
- 2024-1-9: Chest, abdomen CT still near CR status
- In good response 20 months after starting EV+P

Impression:
compatible with multiple lung metastasis S/P treatment, without interval change
For detail, please read the above descriptions.

Reported By SHEN SHU HUEI(LICENSE #: RD555)
On:2024/01/09(19:17:32),(by SHEN SHU HUEI)At:RM505G

Impression:
compatible with left ureter urothelial carcinoma with metastatic lymphadenopathy, S/P treatment, with regressive change and stable as compared with previous film
For detail, please read the above descriptions.

Reported By SHEN SHU HUEI(LICENSE #: RD555)
On:2024/01/04(19:50:45),(by SHEN SHU HUEI)At:RM505G

CR, complete response; CT, computed tomography; EV, enfortumab vedotin; P, pembrolizumab.

It is important we understand the safety profile of EV+P to stay ahead of AESIs

Skin toxicities[1,2]

Incidence: 70%
Grade ≥3: 17%

Severe skin reactions:[1]

1.7 months

Range: 0.1–17.2 months

Peripheral neuropathy[1–3]

Incidence: 63.2%
Grade ≥3: 6.8%

Grade ≥2:[3]

6 months

Range: 0.3–25 months

EV-302 trial exclusion criteria:[4]

Ongoing sensory or motor neuropathy Grade ≥2

Hyperglycaemia[1–3]

Incidence: 13.0%
Grade ≥3: 8.9%

Any grade:[3]

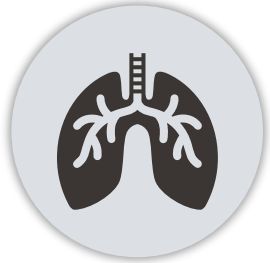
0.5 months

Range: 0.3–3.5 months

EV-302 trial exclusion criteria:[4]

Uncontrolled diabetes, defined as HbA1c ≥8% or HbA1c 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained

Pneumonitis/ILD[1,2]



Incidence: 10.3%
Grade ≥3: 3.5%*

Any grade:[1]

4 months

Range: 0.3–26.2 months

EV-302 trial exclusion criteria:[4]

History of idiopathic pulmonary fibrosis, organising pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis

Ocular AEs[1–3]

Incidence: 21.4%

EV-302 trial exclusion criteria:[4]

Active keratitis or corneal ulcerations

Median time to onset

Disclaimer: PADCEV (enfortumab vedotin) can cause severe skin reactions, including SJS and TEN (predominantly during the first cycle of treatment).

*Two patients experience a fatal event of pneumonitis/ILD.[1]

AE, adverse event; AESI, adverse event of special interest; EV, enfortumab vedotin; HbA1c, glycated haemoglobin; ILD, interstitial lung disease; P, pembrolizumab.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. KEYTRUDA® (pembrolizumab). Summary of Product Characteristics; 3. Brower B et al. *Front Oncol* 2024;14:1326715;
4. Powles T et al. *N Engl J Med* 2024;390:875–888 (protocol).

Pneumonitis/ILD: Risk factors and monitoring

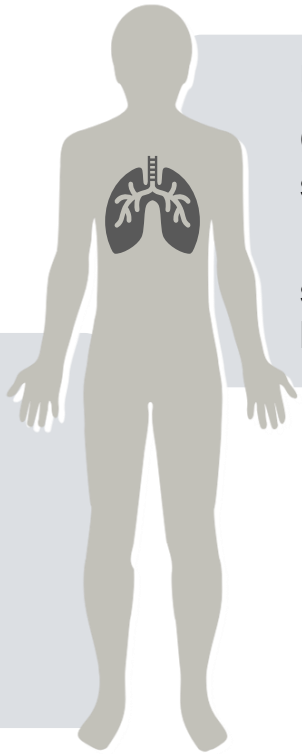
Median time to onset of pneumonitis:[1]

4 months

Pneumonitis/ILD is associated with EV+P, as well as both EV and pembrolizumab as monotherapy; it may be severe, life-threatening or fatal and occurs at a higher rate during combination therapy[1]

General risk factors[1]

- Prior thoracic radiation (immune-mediated pneumonitis)
- History of underlying pulmonary disease



Prevention[1]

Careful monitoring for any signs or symptoms

Patient education on the symptoms they should immediately raise with their healthcare provider

Symptoms and routine monitoring[1,2]

Monitor patients for signs and symptoms, such as hypoxia, cough, dyspnoea, or interstitial infiltrates on radiological examinations

Specialist referral[1]

For severe pneumonitis/ILD, consider referral to pulmonology (if available) for consideration of bronchoscopy and further workup[1]

EV, enfortumab vedotin; ILD; interstitial lung disease; P, pembrolizumab.

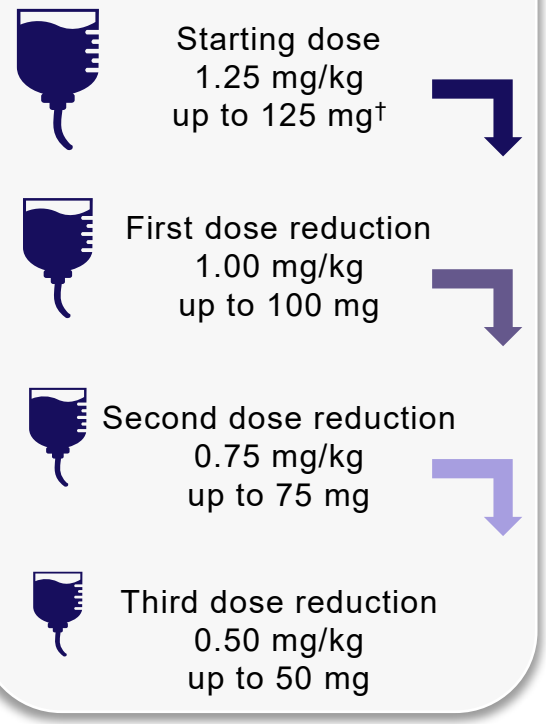
1. Brower B et al. *Front Oncol* 2024;14:1326715; 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

There is established guidance for the management of pneumonitis with EV+P

AESI	SmPC management guidance
Pneumonitis/ interstitial lung disease	Grade 2: Withhold until Grade ≤1, then resume at the same dose or consider dose reduction by one dose level (see right)
	Grade ≥3: Permanently discontinue

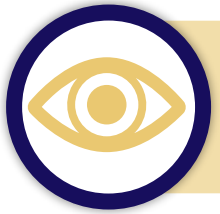
- Use of corticosteroids, immunosuppressive agents, and supportive care should be provided as clinically indicated, and a referral to a pulmonary specialist should be considered*
- When rechallenge is considered, EV may be more suitable for the first rechallenge, given the lower likelihood of serious AE (Grade 3–4)*

Dose reduction schedule

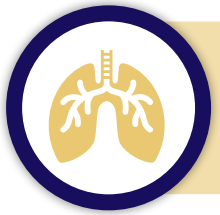


*Speaker's expert opinion; †Up to a maximum of 125 mg for patients weighing ≥100 kg.
AE, adverse event; AESI, adverse event of special interest; EV, enfortumab vedotin; P, pembrolizumab; SmPC, Summary of Product Characteristics.
PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

Summary



Ophthalmology side effects with EV+P are likely related to EV and can be well managed using topical treatment[1]



Pneumonitis from EV+P regimen may be potentially fatal and requires early diagnosis and prompt initiation of corticosteroids, in line with SmPC guidance[1]

EV+P is an effective treatment option; early detection and management of adverse events are important for achieving maximal efficacy for the patient[1,2]

EV, enfortumab vedotin; P, pembrolizumab; SmPC, Summary of Product Characteristics.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics; 2. Brower B et al. *Front Oncol* 2024;14:1326715.

Genitourinary Masterclass

astellas

Please refer to the Korean PI for PADCEV® (enfortumab vedotin) via the following link or QR Code:

<PADCEV 20mg>

<PADCEV 30mg>

Astellas Pharma Korea., Inc.
(7F Parnas tower, 521, Teheran-ro, Gangnam-gu, Seoul, Republic of Korea)

Footnotes